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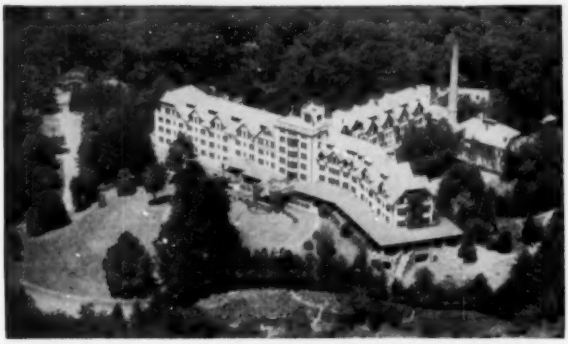

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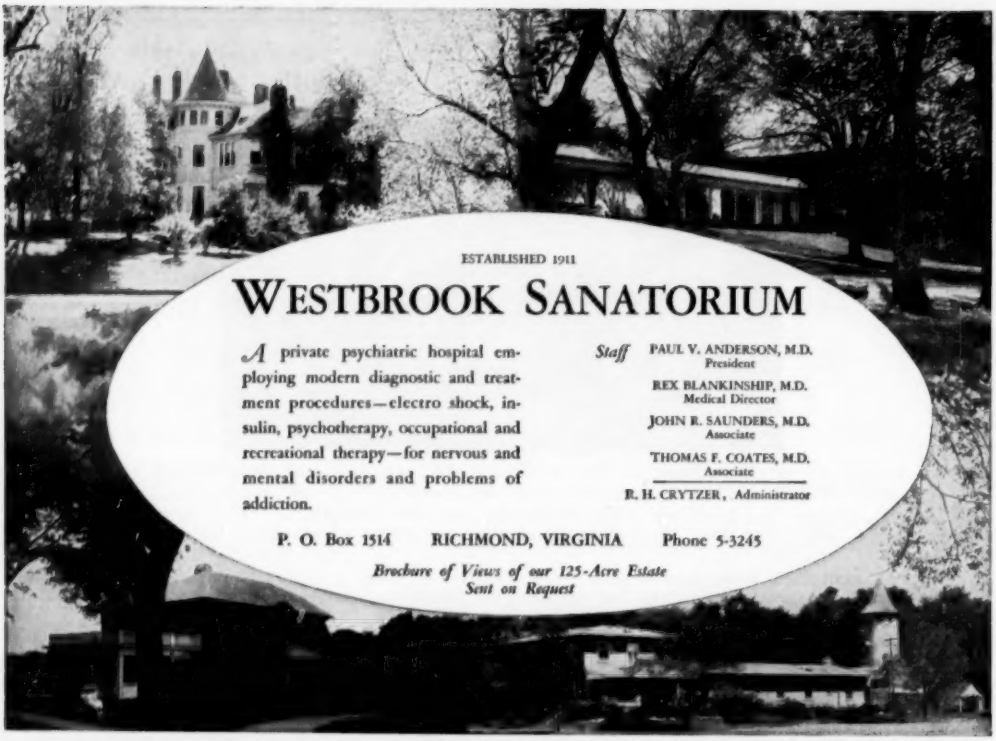

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MANIA IN CHILDHOOD

Report of a Case

JAMES F. McHARG, M.B., M.R.C.P.E., D.P.M.
GLASGOW, SCOTLAND

FUNCTIONAL psychosis is generally believed to be rare in childhood, especially in the prepubertal period, although there is insufficient evidence to exclude the fairly common occurrence of milder forms. In fact, a functional psychosis is seldom considered in childhood unless behavior shows grossly bizarre or incongruous features, when, of course, the tendency is to suspect schizophrenia.

In a series reviewed by Kasanin and Kaufman (1929) of 6,000 admissions to the Boston Psychopathic Hospital, 160 were "children," that is, persons under 16 years of age. Sixty-five of these "children" were psychotic. When their cases were studied and reclassified by the authors, although only 25 were suffering from functional psychosis, as many as 21 of these were considered to be cases of dementia praecox. Potter (1933) described a series of cases of schizophrenia in childhood. Lurie, Tietz, and Hertzman (1936), in a study of 1,000 patients at the Child Guidance Home, Cincinnati, found 20 cases of functional psychosis, and 13 of these were of schizophrenia. Bradley (1945), in fact, asserted that the distinctive psychosis of childhood is schizophrenia. There is, indeed, virtual unanimity that schizophrenia occurs in childhood.

There is, however, no such unanimity about the occurrence and frequency of manic-depressive psychosis in childhood. Much of the literature either describes manic-depressive attacks occurring during the period of puberty or suggests that the condition in childhood proper is very rare, even that it does not occur at all.

Thus, out of the above-mentioned 25 case reports of functional psychosis in "childhood" reassessed by Kasanin and Kaufman, only 4 were considered to indicate a manic-depressive picture. Moreover, all four patients were within the period of pubescence, being aged 15, 15, 14, and 14 years, respectively, and all were subject mainly to the manic phase. The authors observed, "The manic group is fairly clearly cut and the clinical picture is sufficiently well crystallized for us to recognize a typical disorder." There can never have been serious doubt about manic-depressive states occurring at puberty, and the significance of the authors' reassessment of these cases lies, rather, in the fact that they found no manic-depressive illness in childhood proper. A later paper by Kasanin (1931) gave an account of 10 "children" with affective psychosis. Again, most of the patients were at the age of puberty. Four were 15 years old, two were 14, and three were 12. The remaining one was a boy of 11 years who showed a state of excitement. Strecker (1931), in a study of 100 manic-depressive patients, found none whose first attack had been in the first decade

Deputy Physician Superintendent, Glasgow Royal Mental Hospital; Consultant Psychiatrist, Western Infirmary and Notre Dame Child Guidance Clinic.

of life. The earliest age of onset in his group was that of a Russian Jewish girl, who had her first psychotic episode (a depressive one) at the age of 12. Rice (1944) described a boy of 14 who showed manic features. He was of high intelligence, postpubertal, and his illness was related to a love affair. Olkon (1945) described a case of manic-depressive psychosis in a girl of 16, and also a manic illness in a girl of 11 who, despite her age, showed macrogenitosomia and had already been menstruating for a year.

Of those who imply that manic-depressive psychosis in childhood does not exist, Lurie, Tietz, and Hertzman (1936) found not a single case of manic-depressive psychosis in their series of 20 cases of functional psychosis in childhood. Bender and Schilder (1937), in a study of 65 child patients (18 of them under 13 years) with suicidal preoccupations, found that none of them were manic-depressive. The authors concluded that psychotic depressions must be rare in childhood. Bradley (1945) states that he does not believe that true depression occurs at all in children—manic-depressive psychosis, he says, is of rare and questionable existence before puberty. In particular, he states that mania, although reported in a few children in the upper range of childhood (11 and 12 years), is not accepted by a number of careful and experienced workers as occurring in children. He further states that in children sustained elevation of mood and exhilaration are not encountered except in response to reasonably appropriate stimuli. Hyperactivity, he argues, is a frequent symptom of conflict in children but is not observed in attacks that are reminiscent of adult mania. Hyperactivity in children, resulting from emotional conflict, is, he says, usually accompanied by negativism, and to observe it as a pathological symptom in conjunction with an exhilarated emotional response would be a most unusual experience and well worth reporting. Bradley attributes the occasional diagnosis of manic states to faulty observation or faulty interpretation of familiar childhood symptoms. Kanner (1948), in his textbook "Child Psychiatry," does not mention childhood manic-depressive psychosis. Lurie and Lurie (1950) made an extensive survey of the literature on functional psychosis in childhood. On the question of manic-depressive states they cited and agreed with Bradley about its nonoccurrence in childhood. Ituarte and Olaizola (1950) studied 30 cases of "infantile psychosis" requiring hospitalization. Not a single case of "endogenous depression" was seen among them, but it appears that most of their "psychotic" children were epileptic or oligophrenic. Solé-Sagarra (1951) stated that endogenous psychosis in children is rare. In fact, of 600 patients at the children's unit, Barcelona, he found only 1% to be schizophrenic, and there were no manic-depressive or paranoid patients. Hall (1952), in a study of 1,000 patients between the ages of 5 and 16 years, diagnosed "affective" illness in only 6 of them. Only two of these were manic-depressive, and both of them were over 13 years of age.

However, some authors concede the existence of true manic-depressive states in childhood proper. Kraepelin (1921) found that manic-depressive psychosis tends to be rather earlier in its onset than schizophrenia, a fact which is perhaps insufficiently realized nowadays. He said that although the greatest frequency of first attacks was in the "period of development with its increased excitability," between the 15th and the 20th year, yet in rare cases the first manifestations could be traced to before the 10th year. He found that 0.4% of first attacks of manic-depressive psychosis occurred in the first decade of life. In view of this dictum one would expect to encounter cases of manic-depressive psychosis in childhood. Gillespie

(1939) said that it was his impression that manic-depressive psychosis in childhood is rarer than schizophrenia and more difficult to detect. Henderson (1950) also says that clinical experience suggests that manic-depressive psychosis in childhood is rarer than schizophrenia "unless one includes any transient mood disorder under this heading." The paucity of reference in the literature does indeed suggest that manic-depressive psychosis is, perhaps for several reasons, less often diagnosed than schizophrenia. Thus Campbell (1952), in a thoughtful paper, says that he believes that overemphasis is often placed on environmental and "dynamic" factors in the psychiatric illness of children. He thinks there is a tendency to classify the milder cyclothymic reactions in the psychoneurotic category. Certainly the very coherence of the picture in a mild manic-depressive psychosis can lead to specious interpretation in terms of psychodynamics. On the other hand, Campbell thinks that the severer manic-depressive reactions tend to be classified mistakenly as schizophrenia. This is perhaps specially so in "mixed states" (in the Kraepelinian sense) by reason of the incongruities inherent in such conditions. Probably, also, some of the episodic obsessional states of childhood are, in essence, depressive equivalents.

According to Strecker (1921), melancholia in children was first described by Berkham in 1750. Strecker himself studied 5,000 consecutive admissions to hospital and found 18 cases of psychosis in children under the age of 15. Ten of these were manic-depressive patients. In 7 of these 10, the depressive element was most pronounced, but only 1 was frankly manic. Nine of the patients were in the pubertal age group, however, and only one was as young as 10 years of age. Kraepelin (1921) cited Friedman as describing "mild forms" of manic-depressive psychosis in young persons and stated that Liebers had described a case of mania lasting six months in a boy under 5 years of age. Bleuler (1934) stated that individual cases may go back to childhood. Delmas (1937) described at a meeting a manic boy of 16 who before the age of 14 had for several years suffered from obvious short depressive phases two or three times a year. He thought that infantile cyclothymia was common and occurred as early as the age of 2 or 3 years. One such case lasted from infancy until the age of 22. At the same meeting Corberi agreed with Delmas and cited the case of a boy of 9 years who had been hypomanic for some months. A similar case, a boy of 9½, was also mentioned. Dussik * (1934) described the case of a boy of 11 with adiposity and genital retardation who had acute manic episodes alternating with periods of depression. Gillespie (1939) mentioned that occasionally in a manic-depressive subject one has retrospective evidence of a depression before the age of 10. He also mentioned the suggestive finding that of suicides before the age of 15, one-fifth occur before the age of 13. He reminded us that Esquirol and some French authors claimed that manic-depressive states were not uncommon. Two of Esquirol's patients, aged 8 and 9, respectively, had shown a manic picture. Another of Esquirol's patients, a boy of 11, had shown "melancholic symptoms," but Gillespie was skeptical about the assessment of this case. He cited Baruk and Gévaudan (1937) as describing two boys, aged 4½ and 5½, respectively. The first boy suffered from episodes of excitement, lasting for three weeks and recurring at intervals of two weeks. Janota (1948) reported one case (a child of 7) under direct observation. He also gave retrospective reconstructions of four cases starting at the ages of 10, 6, 12, and 7, respectively. All these cases

* Cited by Lange-Cosack.

showed apparently a mild form of the depressive phase, a "forme fruste." Janota felt that cyclothymic oscillations may balance out during puberty. In this connection it may be mentioned in passing that the study already referred to, by Strecker (1931), did not confirm the comparatively poor prognosis which was supposed to be associated with an early onset of manic-depressive psychosis.

Interest in childhood manic-depressive states has been increasing, and an issue of *The Nervous Child* has been devoted to the problem. Most recent studies, however, have been of depressive states—partly, perhaps, because depression as a rule is more obviously morbid than elation—and one difficulty in assessing such cases is that many of the milder depressive states can easily be interpreted, rightly or wrongly, as purely psychogenic, at the cost of ignoring the genetic, constitutional, "endogenous" factor. Schachter (1952), however, described one case of cyclothymic disturbance occurring in a child, noticed first when the child was 2 years of age. He was unable to detect any connection between the clinical state of the child and its emotional relationship to its parents or environment. The child was observed over a period of five years. The author recommended continued long-term observation in such cases. Harms (1952) discussed 10 cases. Most of them were of the depressive type. Although he believed that environment played a considerable part in all his cases, he urged the necessity for recognizing manic-depressive disease in childhood as a psychiatric entity. Sadler (1952) described six children who showed hyperactivity and who grew into definite cycloid personalities. He said they tended to be the "round-face type," and he claimed that they were made normal by phenobarbital. He thought that a constitutional type and a reactive type could be distinguished. Despert (1952) made a study of suicide and depression in children and carried out a statistical analysis according to age levels and yearly trends. She reviewed 400 consecutive cases and concluded that suicidal attempts were more commonly impulsive in nature than the result of rumination. Nevertheless, she also concluded that depression in children is not uncommon. The question of mania in childhood was not raised. Bellak (1952) cited Gareiso and associates (1940) as describing four depressive children between the ages of 11 and 13 years; Beres and Alpert (1940) as describing a prolonged hypomanic episode in a 5-year-old child, who, however, also had signs of organic brain disorder; Stürup (1932) as describing very short phases of mania and depression in a 13-year-old patient, and Cronick (1941) as describing a depressed child of 8. Creak (1952), in answer to an inquiry, said that she would use the terms (*a*) manic-depressive and (*b*) neurotic depression. She thought that in childhood there were, in fact, forms of manic-depressive psychosis, but that below the age of puberty they were exceedingly rare. Creak accepted the Freudian view of manic behavior and said that she had seen two children who appeared to be manic. One, however, was a defective boy and the other was recovering from some form of encephalitic illness, so that one would require further details before accepting these cases as straightforward manic reactions.

Campbell (1952) over a period of four years studied 18 cases of manic depressive psychosis "in children." Most of them were between the ages of 13 and 19, however, and only three were actually in the prepubertal age group, being aged 6, 7, and 10, respectively. However, four others gave a history which extended back into this period. Six out of this total of seven cases of prepubertal onset showed the depressive phase only. The seventh child was described as having been "cyclothymic"

since the age of 6. Campbell emphasized the frequency and importance of manic-depressive states in childhood. He stressed their strong familial tendency and their reversible nature.

Further detailed accounts of functional psychosis in the prepubertal period of childhood are called for—especially of the supposedly rarer, viz., the manic-depressive forms. The rarest form of all, mania, the existence of which is doubted by many, is of particular interest. It is of interest not only to psychiatrists but also, because of its similarity to chorea, to pediatricians and general practitioners. In the literature, there are practically no detailed accounts of manic states in the prepubertal period. It is for this reason that I report the following case of a prepubertal girl of 11, who had a typical manic episode lasting eight weeks, followed by a severe agitated depressive state lasting for an equal period and ending in recovery.

REPORT OF CASE

Margaret B., aged 11, schoolgirl.

Complaints.—The patient herself had no complaints and, in fact, did not recognize that she was ill in any way.

Family History.—There was a positive family history of manic-depressive psychosis on the mother's side. The maternal grandmother was described as "a tartar." She was a staunch supporter of the Salvation Army and was said to be an emotional woman. The mother herself showed no signs of excessive mood swings, but her brother had been subject to recurrent manic-depressive episodes requiring mental hospital treatment.

There was no history of mental illness on the father's side, although he himself, a chef, is a worrier and has a peptic ulcer.

The patient is the oldest of three children. Her brother is of a placid temperament but slightly backward at school, supposedly because of defective eyesight. The youngest child, a sister, was born when the patient was 6 and, although also a placid child, was troubled with occasional enuresis.

Personal History.—The patient had a normal infancy and childhood and was born and brought up in a happy, stable home environment. She had been doing well at school. Although by nature she was an outgoing, happy child, she was overconscientious and had difficulty in tolerating blows to her self-esteem.

General Health.—At the age of 10 months the patient had to go into a hospital because of bronchopneumonia, pink disease (erythredema polyneuropathy), and a poisoned finger. She was in for eight weeks, and after the acute phase had passed she seemed quite contented. She had had several of the common ailments of childhood. At the age of 8, she had been in bed for two weeks with an illness which was said to be "rheumatism." It was described as being "not serious," however, and may, in fact, have been a depressive equivalent.

Prodromal Phase.—For some six months before the onset of the illness, although nothing unusual was noted during the day, the patient was apt to talk, cry, and sometimes walk, in her sleep. There was a retrospective suggestion that during this period the patient had been approached sexually by an elderly man in the neighborhood, who was well known to behave in this way. There was no interference, although indecent exposure may have occurred.

Onset of the Manic Phase.—The onset of the manic phase of the illness was two or three weeks before she was due to sit for the qualifying examination and was fairly sudden. The patient became strange in her behavior and conversation. Her mother said "she became a different person." She was always fidgeting. At night-time she kept coming out from the bedroom to the living room to look at the clock. She would eye it, cocking her head from side to side, and make calculations and comments on how long a sleep she would have. Her father described her condition as follows: "She went carefree, as if she wasn't bothered. She wasn't serious with life. It looked like—well, you know, when some people take a glass of sherry. She went all la-de-da, as if she was putting on an act. It was a 'couldn't-care-less' sort of style . . . quite a comedian act."

The child talked continuously and was very elated. She did not pay attention to her mother or to her teacher and became disobedient and rude. If told to do a thing, she appeared to forget and would go and do something else. If checked for disobedience, she would clap her hands to her head and complain of great pain. Her brows would furrow; her face would become red, and she would ask to go to bed. However, in a few minutes the pain would have gone away.

Her appetite was strikingly better than usual, and her bowels moved more frequently.

On Sunday, March 30, after she had been in this elated, talkative, restless state for a week, she was sent on an errand. However, she spent the money she had been given on ice cream for her sister and herself. She had never failed to bring back a "message" before. Again, when questioned about it, she complained of a headache and asked to go to bed.

The mother felt that things had gone far enough. On the following day the family doctor was called in and said that the child was very ill. She was kept in bed for about a week in the hope that she would be able to sit for her examination. It was found, however, to be difficult, if not impossible, to keep her in bed, as she was always getting up, and she talked continuously. She took a particular interest in colors. When the doctor came, she would be looking out of the window to see the color of his car. Later on a pediatrician was called in. Because of her restlessness chorea was suspected, and his advice was for her to be kept in bed for a longer period. Eventually, however, she had to go to the hospital and was admitted there on April 24, 1952.

Royal Hospital for Sick Children, Glasgow.—On her admission to the hospital the complaint was of "fidgeting and chattering." It was noted that she was a well-nourished child who was extremely restless and talked incessantly.

Her general health was good. Her appetite had been good and her weight steady. The bowels were regular and there was no disturbance of micturition. She had no cough. She had never dropped objects she was holding. In spite of the great restlessness, there were no true choreic movements. The Wassermann reaction was negative. An x-ray of the skull was normal; the optic fundi were normal, and all reflexes were normal.

During her stay of just over three weeks in the hospital the patient was described as continuing to be very restless. She would sing at night. Sedation with phenobarbital, 1 grain three times a day, did not seem to be sufficient, and the dose was increased to 2 grains twice daily. Even with this dose she was not at all drowsy. On the contrary, she slept little but was never tired. During her first few days in hospital she got out of bed several times and on one occasion got into bed beside another patient. She would also take her clothes off at times and sit naked in bed. She gave the impression of being very intelligent. She listened to all that was said near her and "interpolated comments satirically." Her behavior was described by the house physician as being "reminiscent of exhibitionism and extroversion." The doctor noted also that "one would almost say she had 'flight of ideas.'"

Psychiatric Consultation.—I was first asked to see the patient on May 7, 1952, while she was in hospital and when she showed the typical picture of a manic state, viz., psychomotor overactivity, sustained elation of mood, and flight of ideas.

She was a well-nourished, rosy-cheeked, round-faced girl, who got out of her cot and walked about the ward in a completely self-possessed manner. Her attention was continuously being distracted by the behavior of the other children, and she seemed to notice and comment on everything that was said or done. She was taken to a side room, laughing, smiling, and singing or talking the whole time.

In her mood, she was clearly in a state of continuous elation and laughed uproariously from time to time in a very infectious manner. On being questioned, she agreed that she felt very happy.

There was some pressure of talk and flight of ideas. She made frequent puns and told many jokes appropriate to her age. She sang snatches of songs, breaking off in the middle of a tune to continue her chatter. There was a striking absence of normal shyness and she began the interview by making comments about the doctor's appearance, showing again a special interest in colors.

She glanced at the doctor's blue tie and exclaimed, "What a tie!" Quickly looking downward, she said with a laugh, "and look at his socks! Blue!" Then, looking out of the window at the green trees and grass, she went on, "Blue and yellow make green." Still looking out of the window, she said, "Shall I tell you a dirty story? A man fell out of a window into a heap of soot!" Here the patient rocked herself in the chair with laughter.

The content of her utterances was confined to comments on her immediate surroundings and to associations from them of a general, but witty, kind. She was not able to concentrate sufficiently to speak about home or of her life before going into the hospital. There was no evidence of hallucinations or delusions. She seemed to be aware that she was in a hospital but was not sure what day it was. Her attention could not be kept on what obviously seemed to her to be trivial and unimportant matters. Her memory was difficult to test but was unimpaired so far as one could tell. Concentration, however, was impaired by reason of her great distractibility.

She seemed to be of at least average intelligence but had no insight into the fact that she was ill.

Duration of the Manic Phase.—In all, the manic phase lasted for approximately eight weeks.

The Depressive Phase.—During the patient's last two or three days in hospital she was noted to be much quieter and "rather depressed." She was discharged home on May 18, 1952, on the understanding that she attend at the psychiatric outpatient clinic. At her first attendance her father reported "she breaks out into these depression fits, worrying about exams and spelling and so on." The patient herself, when seen, was reluctant to speak to the examiner. She clung to her mother, weeping loudly and saying that she was "the cause of the world going to be destroyed."

The girl was so distressed that the question of admission to a mental hospital was considered. The mother, however, preferred to try to manage her at home. For a month she was allowed to sleep in her parents' room. She was brought, reluctantly, to the clinic once or twice and was always very distressed.

Four or five times a day she had attacks of crying and screaming, when she appeared "haunted" and overcome with fear. These would last about 15 minutes. She would cry and say, "What have I done, Mummy? I must have done something wrong for God to be angry at me." "Oh Mother, Mother, there it comes again"; then, "Oh, it has gone," or "Something is going to happen" and "What is going to happen to the world?" She also seemed to realize that something was the matter with her and said God was punishing her and she wanted to die. She was always wanting to sit on her mother's knee, not allowing the mother to be out of her sight night or day. She would fondle her mother's hair and say, "Beautiful, beautiful; it smells beautiful." She had to be dressed, washed, and fed, although she ate fairly well. She did not want to go out, only to look out of the window, and she was disinterested in everything around her. She would frequently ask, "Are we real?" If persuaded to go out or if she met anyone she knew, she cried to go home, and she did not seem to recognize the neighborhood or where she was. She constantly twiddled her hair with her fingers and bit her nails to the quick. She seemed very depressed, had a vacant look, and was not interested in books or comics. Her father could get her to go only to the door and could not get her interested in the garden. He got her a bicycle and eventually persuaded her to go for a little way up and down the road, but only if he walked with her.

Phase of Recovery.—During August, the family took a holiday and went for bus tours and steamer trips. The patient seemed to begin to enjoy these, and it was noticed that she always had her ears "cocked" for conversation between her parents. Eventually she improved sufficiently to go out for "messages" and to do odd jobs in the house. She even went swimming and to the pictures.

She was seen after her recovery at her own home on Sept. 27, 1952, and her parents said she was quite well. She seemed, indeed, to be happy and was playing with the other children. She did not remember me, and her parents said that she had no recollection of her stay in the hospital.

Duration of the Depressive Phase.—As closely as could be judged, the depressive phase lasted for a period equal to the manic phase, viz., eight weeks.

Subsequent History.—She was seen from time to time in her own home during subsequent months. She returned to school and remained well.

She menstruated for the first time in July, 1953 (nearly a year after the end of her illness), and there was no attendant emotional upset.

When she was seen in September, 1953, she showed a certain normal shyness at first but later on began to talk spontaneously about school affairs. She had been at the top of her class and had won an award for swimming. She remembered my previous visits to her, with the exception of her time in the hospital. It was felt wise not to probe too much or to attempt to obtain a retrospective account of her feelings during her illness.

Her home was visited on Feb. 13, 1954, but she was out at the cinema. Her mother reported that she was keeping well. At school she was excelling, "Everything she puts her hand to she comes top in." She was still sensitive, however, and apt to cry if reproved for a minor fault.

COMMENT

The case is that of a prepubertal girl, aged 11, who had a psychotic illness lasting for 16 weeks.

The illness was characterized by a fairly sudden onset, and it ran a circumscribed course, ending in complete remission.

The reaction was a total psychotic one in the sense that it involved every psychobiological level. During the first eight weeks of the illness this was shown by the general appearance of glowing physical health, the increased appetite and bowel activity, and the remarkable tolerance for phenobarbital. The mental features were those characteristic of mania, viz., a sustained exaltation of mood, marked psychomotor overactivity, and flight of ideas.

The supposed rarity of mania in childhood was the one fact which caused hesitation at the time in making the diagnosis. Chorea was excluded by the absence of true choreic movements. There were no physical findings to suggest encephalitis or other forms of brain disease. Mental defect and organic dementia were out of the question, and there were no schizophrenic features.

The clinical features were not those of a psychoneurosis, in fact, environmental factors seemed to have little bearing on the onset, progress, or termination of the illness. The home background was affectionate and stable and, although the girl was worried about examinations, her school record was excellent. The significance of the supposed episode of indecent exposure by the elderly man was problematic. Psychoanalytically, one could interpret the manic reaction as elation at the gratification (in fantasy) of an incestuous wish toward the father, represented by the elderly man, and the depressive reaction as subsequent guilt and punishment for the same.

Confirmation of the diagnosis of mania came from the family history of manic-depressive psychosis, from the fact that the second eight weeks of the psychotic period were characterized by typically depressive features, and, finally, from the fact that complete remission occurred without any special psychotherapy.

SUMMARY

The occurrence of functional psychosis in the prepubertal period of childhood is discussed with reference to manic-depressive psychosis, and particularly to states of mania. The relevant literature is surveyed.

An attack of mania (followed by a depressive phase), occurring in a girl of 11 over a year before the onset of menstruation, is described and discussed.

Dr. J. H. Hutchison, O.B.E., and his assistants at the Royal Hospital for Sick Children, Glasgow, gave permission to refer to their case notes, and Mrs. J. Lomax (psychiatric social worker) gave help in the study of the case.

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CLINICAL ASSESSMENT OF PASSIVE-AGGRESSIVE PERSONALITY

ROY M. WHITMAN, M.D.
HARRY TROSMAN, M.D.
AND
RICHARD KOENIG, M.D.
CHICAGO

THE DIAGNOSIS "passive-aggressive personality" in 1945 was incorporated into a War Department Technical Bulletin [1] which dealt with medical nomenclature. The Veterans Administration used this nomenclature experimentally in several large psychiatric centers and, on the basis of uniform approval from these centers, recommended its adoption in 1946. The Committee on Nomenclature and Statistics of the American Psychiatric Association, utilizing this experience, published a new "Diagnostic and Statistical Manual [for] Mental Disorders" in 1952.[2]

In this diagnostic manual, passive-aggressive personality is a subdivision of personality trait disturbance in which neurotic features are relatively insignificant and the basic personality maldevelopment is the crucial distinguishing factor.

The manual lists three subdivisions of passive-aggressive personality: passive-dependent type, passive-aggressive type, and aggressive type. These personality types are described in the manual as follows:

> Passive-Dependent Type: This reaction is characterized by helplessness, indecisiveness, and a tendency to cling to others as a dependent child to a supporting parent.
>
> Passive-Aggressive Type: The aggressiveness is expressed in these reactions by passive measures, such as pouting, stubbornness, procrastination, inefficiency, and passive obstructionism.
>
> Aggressive Type: A persistent reaction to frustration with irritability, temper tantrums, and destructive behavior is the dominant manifestation. A specific variety of this reaction is a morbid or pathological resentment. A deep dependency is usually evident in such cases.[2]

In this paper when we are considering the generic group, we shall use the term passive-aggressive-dependent (P. A. D.). When we refer to the subgroups, we shall use the terms passive-aggressive (P. A.), passive-dependent (P. D.), and aggressive (A.).

PURPOSE

The purpose of this study was to examine the operational use in a psychiatric outpatient clinic of the diagnostic category passive-aggressive personality. The questions considered were these: 1. How was the diagnosis understood by each of the participating psychiatrists? 2. Were there any personality attributes other than those described as passive-aggressive behavior? 3. Were there any consis-

Division of Psychiatry, University of Chicago Clinics.

tent psychodynamic implications underlying the descriptive nature of the diagnosis? 4. Was the diagnosis of sufficient importance to influence a psychotherapeutic plan independent of other factors? 5. Could amendments and changes be suggested to improve communication and use?

PROCEDURE

In 1952 the "Diagnostic Manual" of the American Psychiatric Association was adopted by the Outpatient Clinic of the Division of Psychiatry of the University of Chicago Clinics. Previous experience with the type of patients who had presented themselves to a general hospital outpatient clinic indicated that the majority of these patients complained of specific symptoms which were interpreted as a reaction to an immediate stress situation. These symptoms were the chief basis for the "clinical reaction type." We extracted from the "Diagnostic Manual" as the clinical reaction type the diagnoses listed in all the categories excluding personality disorders, namely, psychotic reaction, chronic brain syndrome, psychophysiological reaction, and types of psychoneurotic reactions.

An attempt was made to describe the underlying personality as personality pattern disturbance or personality trait disturbance. This approach of reaction type superimposed on personality disorder was analogous to the "qualifying phrase" method described in the "Manual" of the American Psychiatric Association. Our method was favored because of the emphasis in brief psychotherapy on the current situation and its precipitating stresses.

The conceptual framework was similar to that described by Menninger,[3] in that our fundamental interest was in identifying the external threat, the activated internal impulses, and the defenses against these impulses. Our therapeutic orientation was toward a brief psychotherapeutic program (about 4 to 12 interviews) where this was suitable. The procedure did not eliminate the use of prolonged psychotherapy, psychoanalysis, hospitalization, or any of the other therapeutic maneuvers and dispositions which are the usual armamentarium of the psychiatric outpatient department. The brief psychotherapeutic orientation made possible a degree of relationship greater than that of a diagnostic one with a large number of patients. The basic principles of brief psychotherapy included flexibility, manipulating the frequency of interviews, emphasizing current reality, and concentrating largely on a significant sector during psychotherapy.[4] In addition, a collaborative psychotherapeutic approach was often employed with a significant relative, who was seen by the psychiatric social worker.*

DATA

In the year 1952-1953, a total of 400 patients were seen in the outpatient clinic. Reaction types are shown in Table 1 and are based on the presenting clinical picture during the psychiatric interview, as well as on the history of the chief complaint and present illness.

Table 1 indicates that for the predominant number of patients the clinical diagnoses were of the depressive reaction type, the next largest category being anxiety reaction. Schizophrenic reaction was the third highest category, but only 8% of the sample. These data give an indication of the type of population examined in this study; i. e., almost 90% of the diagnoses were in the psychoneurotic category.

In accord with our previously designated system of two diagnoses, Table 2 indicates the basic personality diagnosis. The personality type was a descriptive diagnosis based on the behavior during the interview and on the reported behavior

* Whitman, R. M., and Young, I. S.: Psychiatric Social Work in a Brief Therapy Program in an Adult Outpatient Clinic, read at the 31st Annual Meeting of the American Orthopsychiatric Association, New York, March 12, 1954.

from the life history of the patient, usually taken from the patient. In addition, in approximately 20% of the cases an auxiliary description was obtained by a psychiatric social worker from a significant relative.†

Thus, we see that the passive-dependent personality was the largest category (23%) and with the passive-aggressive type (15.5%) constituted the largest number of personality disorders (38.5%). We found it helpful to use additional terms, such as hysterical and masochistic personality. These we felt were easily communicable and could not be subsumed under any of the categories listed in the

TABLE 1.—*Clinical Reaction Types in 400 Cases*

	No. of Cases	%
Depressive	135	34.0
Anxiety	109	27.0
Schizophrenic	32	8.0
Psychophysiological	23	6.0
Situational	23	6.0
Phobic	17	4.0
Special symptom	11	2.5
Conversion	10	2.5
Chronic brain syndrome	10	2.5
Other types *	30	7.5
Total	400	100.0

* Paranoid, 6; obsessive, 5; dissociative, 4; hypochondriacal, 4; other psychosis, 4; narcolepsy, 4, and not diagnosed, 3.

TABLE 2.—*Basic Personality Diagnoses*

	No. of Cases	%
Passive-dependent (P. D.)	92	23.0
Hysterical	78	19.5
Schizoid	76	19.0
Passive-aggressive (P. A.)	62	15.5
Compulsive	32	8.0
No diagnosis *	21	5.25
Masochistic	13	3.0
Cyclothymic	2	0.5
Aggressive	1	0.25
Other types †	23	6.0
Total	400	100.00

* Primarily chronic brain syndromes in which the underlying personality was obscure.
† Inadequate, antisocial, dissocial, etc.

American Psychiatric Association "Manual." In the case of the passive-dependent and passive-aggressive personalities, however, we adhered closely to our understanding of the diagnoses described in the "Manual."

In Table 3, the clinical reaction types occurring in the personality diagnoses of passive-aggressive and passive-dependent and in the total 400 cases are compared.

It is evident from Table 3 that in the passive-aggressive personality the chief clinical reaction type is anxiety reaction, while in the passive-dependent person-

† Whitman, R. M., and Young, I. S.: Psychiatric Social Work in a Brief Therapy Program in an Adult Outpatient Clinic, read at the 31st Annual Meeting of the American Orthopsychiatric Association, New York, March 12, 1954.

ality the chief clinical reaction type is the depressive reaction. It is striking that there is an absence of schizophrenic reactions, and a larger percentage of psychophysiological reactions, in the P. A. D. category.

Table 4 is a comparison of the male-female population distributed among passive-aggressive (P. A.), passive-dependent (P. D.), and hysterical categories and the total 400 cases.

In Table 4 we see that among the generic group, passive-aggressive-dependent (P. A. D.), there were significantly (at the 0.01 level) more males than females as compared with the total patient population. This was more pronounced, however, in the passive-aggressive (P. A.) subgroup than in the passive-dependent (P. D.) subgroup. It is interesting to contrast this ratio with the reversal of the sex ratio in the diagnostic category of hysterical personality.

TABLE 3.—*Comparison of Clinical Reaction Types*

	P. A., %	P. D., %	400 Cases, %
Depressive	25	36	34.0
Anxiety	41	29	27.0
Schizophrenic	0	0	8.0
Psychophysiological	11	11	6.0
Situational	10	7	6.0
Phobic	2	7	4.0
Special symptom	6	2	2.5
Conversion	2	4	2.5
Chronic brain syndrome	0	0	2.5
Other types	3	4	7.5
Total	100	100	100.0

TABLE 4.—*Comparison of the Male and Female Population, in Percentages*

	P. A.	P. D.	Hysterical	400
Male	70	55	2	40
Female	30	45	98	60

At intake, the peak age distribution for passive-aggressive personality (P. A.) was in the 31- to 40-year decade, in contrast to the passive-dependent personality (P. D.), which was in the 21- to 30-year decade. The age distribution of the 400 patients was a curve of normal distribution, ranging between the ages of 15 and 70 years, with the fourth decade being the mean.

Stated religious preference revealed significantly more Catholics in the passive-dependent group (0.01 level) than among the total 400 patients, whereas the number of Protestants was significantly greater (0.05 level) in the passive-aggressive category.

Though marital, occupational, and educational status, nationality, and referral source were subjected to statistical analysis, we could find no significant correlations in the data, as contrasted with the entire series of 400 cases.

As is apparent in Table 5, psychotherapeutic plans for the total group of P. A. D. were distributed among the various categories. This distribution was similar to treatment plans for the 400 cases except that we offered interpretive treatment more frequently. Hospitalization was offered less often in the P. A. category than in the P. D. group or the total 400 cases.

As noted in Table 6, termination by the decision of the physician or mutual consent was much commoner in the passive-dependent than in the passive-aggressive personality group. The passive-aggressive personality broke contact after one return visit more frequently than did any other personality type. Both the P. A. and P. D. groups failed to return after the intake interview significantly more frequently than did the 400 patients.

REPORT OF CASES

The following is a case report of a typical patient in the passive-aggressive (P. A.) category.

T. M. is a 36-year-old, married assistant chief of production in a paper plant. He entered the outpatient clinic with the complaint, "I keep imagining that I have heart trouble, but the doctors keep telling me that I don't." His preoccupation with heart disease began at the age of

TABLE 5.—*Comparison of Treatment Plan and Disposition, in Percentages*

	P. A.	P. D.	400
Supportive	45	46	48
Interpretive	27	26	20
Relationship	18	13	10
Preparatory	3	4	4
Environmental change	0	0	3
Hospitalization	0	7	9
Other types	7	2	5

TABLE 6.—*Termination of Treatment, in Percentages*

	P. A.	P. D.	400
Advice of physician or mutual consent	29	41*	33
Termination after one visit without advice	18*	7	11
No return after intake	21*	21*	15
Other reasons (hospitalization, prolonged treatment, etc.)	33	31	41

* Significant (0.05 level) as compared with the value for the 400 patients.

22, when he awoke to find that his heart was beating rapidly. He recalls that his mother and older brother came into his room and remarked that this was the way the patient's father had died when the patient was 7 years old.

In 1942 the patient was drafted. He experienced a good deal of combat in the service, with little anxiety about his heart. During this period he was closely attached to a colonel as an aide, and he stated that he had a good, though distant, relationship with this man. In 1945 the colonel suggested a rest trip to the patient, and the patient became very anxious. On his return, he found that he was no longer attached to the colonel and became panicky. He received an honorable discharge and returned to marry his present wife, whom he describes as a wonderful and understanding woman. He denies marital difficulties and speaks fondly of his two "fine" children.

In civilian life the patient returned to his former position, where he is employed at present. He found that there had been a radical shift in personnel. An older superintendent, with whom he had been fairly close, had left, and an "unreliable man" took his superior's place. The new superintendent put one of his own cronies in the patient's former position, forcing the patient into a job of less prestige. His anxiety concerning his heart mounted. He frequently took his pulse and looked at his lips in the mirror to see if they were cyanotic. He avoided arguments and situations in which he found himself disagreeing with someone openly. Most of his energy was directed into work activities, where he was constantly offering his superiors novel suggestions to increase production.

His behavior during the interview alternated between anxious propitiation and challenging stubbornness.

A diagnosis of anxiety reaction in a passive-aggressive personality was made. The patient seemed to be bothered primarily by hostile impulses toward authoritarian male figures with whom he came into contact at work.

The aim in treatment was to confront him with his hostilities, both in his work situation and in therapy, and to differentiate his hostility from the realistic assertiveness expected in his work situation. His tendency to regress to a passive position was not interpreted. Latent competitive tendencies toward the therapist were highlighted. During the course of 12 hours of therapy the patient became aware of the relation between his anxiety about his heart and episodes at work when his hostility was stimulated. He continued a pattern of regression to a passive position in relationship to authoritarian figures, which he could not accept consciously. His inability to express himself assertively when this was appropriate was related to his hostile feelings toward his father and the dire consequences which seemingly had resulted in the death of his father.

Treatment dealt essentially with the patient's obvious propitiation toward the therapist, which was interpreted as a resistance toward the expression of other feelings. When these hostile competitive feelings became manifest, he was encouraged to express them, and a differentiation was made between aggressivity and pseudoaggressivity.

The following is a case report of the passive-dependent personality type.

W. R. is a 30-year-old photoengraver who complains of depression and "too great a concern with myself." His trouble began in July, 1952, when his brother, with whom he had been living, left town with his family, so that the patient had to take a room in a private house. At this time the patient experienced a hungry, "heartachy" feeling, which was followed in a few months by restlessness, depression, and inability to concentrate. During his period of illness he made frequent trips to his mother, who lives in a small town in southern Illinois.

He was married in 1944 and was drafted in the same year. He adjusted well to the Army, but at the end of the war he found to his bewilderment that his wife wanted a career and had initiated divorce proceedings. In spite of his mild protestations, his wife refuses to allow him to see their 6-year-old daughter, to whom he is deeply attached. At work the patient is apparently highly competent and is given many of the jobs other photoengravers are not capable of doing. This requires extra hours of work without additional pay. He feels that it is his obligation, however, to do this.

His demeanor in the interview was pleading, helpless, and occasionally tearful. There was no show of resentment or hostility in describing any interpersonal relationship.

A diagnosis of depressive reaction in a passive-dependent personality was made. Frustration of his dependent needs (precipitated by loss of the brother) led to a depressive reaction and symptom formation.

He was seen for a total of four interviews over a two-month period. The positive aspects of his personality were dealt with in terms of his desire to help others and his efficiency and competency at work. He was encouraged to make the legitimate demands merited by his superior work. His reliance upon his brother and the significance of the termination of this relationship were clarified. He was told to return to the clinic after termination if he felt the need. When seen six months later, he related that he had improved greatly, had decided to remarry, and was making plans to buy his own home.

These two cases are typical examples of the P. A. D. personality and served, with the rest of the case material, to provide data for the discussion of our results.

RESULTS AND COMMENT

We shall attempt to answer the five questions considered at the beginning of the study.

1. *Communicability.*—A definite confusion existed in the clinical use of this diagnosis. On the one hand, the "Manual" of the American Psychiatric Association implies that the term passive-aggressive describes a particular type of aggression.

An alternate interpretation favored by the majority of our psychiatrists was to use passive-aggressive as a continuum of behavior, the two extremes being passivity and aggressivity.

The other area of confusion was between passive-aggressive as a generic term and passive-aggressive as a subtype.

We used the aggressive type when there was no evidence of sociopathic behavior or any evidence of overt passivity. This state was very rare and may have been a function of the type of patient seen by this clinic.

2. *Personality Attributes.*—The usual characteristics found in the passive-aggressive personality were those of a Protestant man in the fourth decade of life with indeterminate marital, occupational, and educational background. There is some suggestion genetically that there was an intense ambivalent relation to the father, but this is variable. The patient most frequently came in complaining of anxiety.

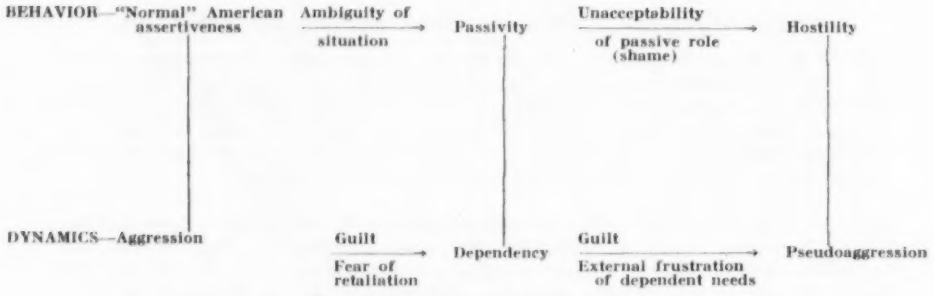

Fig. 1.—Passive-aggressive personality

In the passive-dependent group, the patient was more likely to be a Catholic man in the third decade of life, complaining of depression. No genetic factors were consistent.

3. *Psychodynamics.*—The psychodynamics most frequently found underlying passive-aggressive and passive-dependent personality can be outlined in two diagrams (Figs. 1 and 2). In these diagrams the crucial differentiation is between behavior and the psychodynamic forces underlying behavior.

Figure 1 deals with the behavior and dynamics of the passive-aggressive personality. We see in Figure 1 that aggression is the need, or drive, and is manifested behaviorally by "normal" assertiveness. When the aggression is inhibited by internal guilt or fear of external retaliation, regression to a dependent position occurs. This is revealed by passive behavior. Passive behavior may also be stimulated by inability to deal with the ambiguity of a role requirement, so that assertiveness yields to passivity. The final step, dynamically, would be guilt over dependent needs, or external frustration of these needs, leading to pseudoaggression, the behavioral counterpart being hostility. On the behavioral level, shame over a culturally unacceptable passive role leads to hostility.

Figure 2 deals with the behavior and dynamics of the passive-dependent personality. When dependency needs are stimulated, they may manifest themselves directly as passivity. Dependency may be unacceptable because of internal guilt or

external frustration of dependent needs. This, in turn, may lead to pseudoaggression and manifest itself behaviorally as demandingness. The role of passivity because of its cultural unacceptability and resultant shame may be transformed into demandingness.

In both diagrams behavior and dynamics simultaneously feed into one another, in a series of transactional processes. Behavior influences dynamics, and dynamics, in turn, influence behavior.

In considering the degree of disorganization present, it appears that the passive-dependent personality is more poorly organized and may defend himself only slightly against the emergence of primary impulses. Indeed, defenses may be absent, and passive behavior may manifest itself as an expression of a basic dependency. In the passive-aggressive personality, on the other hand, there is an elaboration of defense which indicates a healthier personality.

We should like to stress that the passive-aggressive axis is a universal pattern. The psychopathological response is a function of the quantitative and qualitative

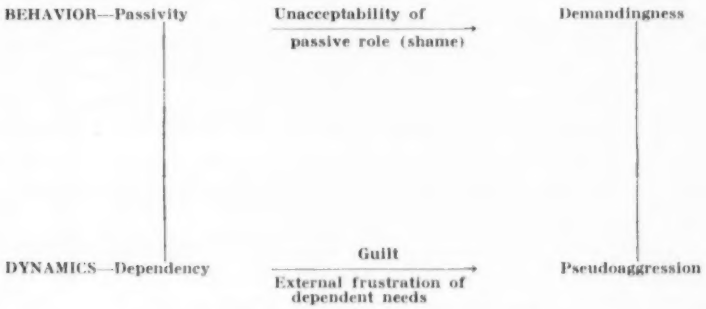

Fig. 2.—Passive-dependent personality

character of the drives and of the appropriateness of these drives to the field. From a perceptual view, the subject must scan the field, determine the role required of him, and be able to accept internally the demands of this role.

It would seem that the diagnosis of passive-aggressive personality in the male has its counterpart in our diagnosis of hysterical personality in the female. This seems to be largely a function of the American culture, in which problems of the male along the axis of dependency and aggressivity are foremost, while in the female problems along the axis of sexuality and dependency are foremost. The American culture positively sanctions the expression of assertiveness in the male and negatively sanctions the expression of passivity. In the female the culture negatively sanctions sexuality and positively sanctions passivity. We found that the females with a diagnosis of passive-aggressive personality were usually those who were working in job situations in which they had difficulties in the hierarchical organizations and were not in home situations. Often the male with passive-aggressive personality came in complaining of job difficulty which was related to the ambiguity of his position in his job situation. In other words, where there is an unambiguous structuralization of roles, expectations of behavior are clear. Thus,

in a peacetime nonconscripted army, where there is an acceptance of defined ranks, the behavioral role is less a problem than in certain "in-between" positions in industry, where the person is not sure of his status.

4. *Psychotherapeutic Plan.*—Interpretive treatment was more frequently recommended for the passive-aggressive-dependent (P. A. D.) group than for any other. Generally, plans for therapy were a function of the severity of the precipitating stress, duration and intensity of symptoms, present environmental situation, motivation to change, and ego strength, rather than one of personality diagnosis.

In interpretive treatment there could be formulated some general principles of psychotherapy of the passive-aggressive and the passive-dependent personality. In the passive-aggressive category, the general plan was to differentiate hostile from assertive behavior and to encourage acceptance of the realistic dependency of the psychotherapeutic situation. Dynamically, the psychiatrist must deal with the patient's fear of aggression and dependency. This must come relatively early on a superficial level, or the patient may discontinue treatment after only a few visits.

In interpretive treatment of the passive-dependent personality, the general goal was to encourage assertion, or even hostility, and not to permit too great expression of passive-dependency, as by decreasing the frequency and number of interviews.

We did not have sufficient experience with the aggressive personality, although we felt that sustained hostility would frequently result in difficulties with social institutions, so that the diagnosis of sociopathic would be more applicable.

In general, it seems that the passive-aggressive personality has a better prognosis than does the passive-dependent personality. This belief is based on the lack of hospitalization in the former group, more complex ego defense patterns, and occurrence of the initial visit at a later age in life.

5. *Suggested Revisions.*—(*a*) There should be a careful distinction made between behavior and dynamics. Assertiveness is a behavioral aspect of aggressivity. Aggression should be reserved for a healthy, normal drive. There should also be a clarification of the terms passivity and dependency. Passivity can be considered a behavioral aspect of dependency. Thus, we suggest that the diagnostic term "passive-aggressive" be changed to "passive-hostile." We suggest, further, that "passive-dependent" be changed to "passive" personality. For the "aggressive" personality, we would substitute the term "hostile" personality.

(*b*) Passive-hostile, passive, and hostile patterns could then be emphasized as truly behavioral diagnoses, with limited dynamic implications and no genetic implications. In this sense hostility can occur at all levels of psychosexual development, and therefore oral-aggressive, anal-aggressive, and phallic-aggressive forces may all underlie the behavioral manifestations of the passive-hostile personality. Similarly, there may be other dynamic forces underlying passivity, such as sexuality, strong regressive trends, and massive withdrawal reactions.

(*c*) The generic term for the three diagnoses should be dropped so as to avoid confusion with the subgroups. We feel that there is sufficient justification to have each of the three behavioral reactions in a separate category; but, if necessary, a superordinate term, such as dominant-submissive personality, could be used.

(*d*) In the making of diagnoses the field must be considered in terms of both the immediate interpersonal field and the larger cultural field. The passive-hostile personality is a personality in close relation to the field. This personality is in

contrast to the compulsive or schizoid personalities, who, in a sense, carry their latent reaction patterns around within themselves and are more independent of their social environment. Linton ‡ colorfully described this concept when he said there are two types of personalities, chameleons and beavers. Chameleons change with the surroundings; the beaver pursues his inner mission. There is also a striking parallel between the passive-hostile personality and Riesman's recent formulation [6] of the "other-directed" personality. Both depend on external cues to guide their behavior.

SUMMARY

In a consecutive series of 400 outpatients, 155 had a diagnosis of passive-aggressive or passive-dependent personality.

Operationally, we noted a confusion in the use of the diagnosis. On the one hand, "passive" was used to describe a form of aggression and, on the other hand, as one pole of a behavioral axis of passive aggressivity.

We have noted a further confusion between behavior and dynamics and have outlined a scheme whereby aggression, dependency, and pseudoaggression are designated as the dynamics underlying the behavior of assertiveness, passivity, and hostility, respectively.

An auxiliary dynamic formulation is necessary to supplement the mainly descriptive diagnosis of passive-aggressive personality in order to formulate a psychotherapeutic plan.

There is no relation between the type of psychotherapy offered and this diagnosis.

The passive-aggressive personality implies a healthier mode of reaction pattern, with a better prognosis, than the passive-dependent personality.

This diagnosis is particularly applicable in the American culture, where a premium is placed on assertiveness in the male and a prejudice is expressed against passivity.

Neurotic reactions occur in persons who have the tendency to respond along a passive aggressive axis in situations of ambiguity or in situations which demand a degree of aggression or dependency which is unacceptable to them.

We suggest as a generic term, dominance-submission, with subheadings of (1) passive-hostile, (2) passive, and (3) hostile personality.

‡ Linton, in Sargent and Smith.[5]

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SUCCINYLCHOLINE CHLORIDE IN ELECTROSHOCK THERAPY

III. Oxygen Consumption and Arterial Oxygen Saturation

W. P. WILSON, M.D.
MONTREAL, CANADA
J. B. HICKAM, M.D.
W. K. NOWILL, M.D.
AND
R. FRAYSER, A. M.
DURHAM, N. C.

IN PREVIOUS publications * observations on the clinical use of succinylcholine chloride and thiopental (Pentothal) sodium in electroshock therapy and the effects of these drugs on cardiovascular reactions have been reported. It was observed that anoxia was not seen in those patients in whom succinylcholine and thiopental were used together and who were given 100% oxygen during shock. Both the use of 100% oxygen and the abolition of muscular activity apparently play a part in preventing the development of anoxia during the apneic period. Because of these observations, we deemed it desirable to attempt to determine what effect premedication had on arterial oxygen saturation and oxygen consumption during electroshock. Although there have been studies † in which anoxia was demonstrated by analysis of arterial blood samples, no quantitative studies have been done relating arterial anoxia and oxygen consumption.

It is the purpose of this paper to quantitate the amount of work done by measuring the oxygen consumption and to determine the blood oxygen saturation curves in subjects receiving unmodified electroshock and in those receiving electroshock modified by thiopental or succinylcholine-thiopental in combination.

METHOD

Sixty-one patients undergoing electroshock treatment at Duke Hospital or the State Hospital at Butner, N. C., were selected for this study. All patients were physically normal and were receiving electroshock at daily intervals or three times weekly. All shocks were given with the

Present address: Montreal Neurological Institute (Dr. Wilson).

From the Department of Psychiatry, Department of Medicine and Division of Anesthesiology, Duke University School of Medicine.

The succinylcholine chloride (Anectine Chloride) used in this study was supplied by the Burroughs Wellcome & Company, Inc., Tuckahoe, N. Y.

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* References 1 and 2.

† References 3 through 5.

Medcraft Electroshock apparatus or the Liberson Brief Stimulus apparatus. Prior to the institution of this study, a comparison was made as to the duration of seizures obtained with the two machines, and these were found not to vary significantly.

For the oxygen consumption studies the patients were prepared for electroshock in the usual manner by withholding food before the treatment. Those patients who were to receive thiopental sodium or succinylcholine-thiopental were given atropine, 0.4 to 0.8 mg., intramuscularly 20 to 40 minutes prior to the treatment. The patients rested for approximately 20 minutes before shock was given. Oxygen consumption was not measured in the preshock period. Immediately after the electroshock an anesthesia mask, fitted to a one-way respiratory valve, was placed over the patient's face. If necessary, an oropharyngeal airway was inserted to maintain good respiratory exchange. These procedures were completed during the postshock apneic period, which usually lasted for 30 to 45 seconds. Exhaled gases were then collected in 30-liter Douglas bags. Serial specimens were collected until respiration seemed normal or the subject's activity made further collection impossible, or until three minutes had elapsed. The average collection period was approximately two and one-half minutes.

This technique of necessity was changed in those patients receiving succinylcholine-thiopental sodium. These patients required artificial respiration. It was therefore necessary to design a special one-way valve which would allow artificial respiration and at the same time permit the collection of expired gases. The valve was designed by one of the investigators (W. K. N.), and was found satisfactory for the purposes of this study. Pure (100%) oxygen was used for

Mean Oxygen Consumption and Carbon Dioxide Output During the Two- to Three-Minute Period Following Seizures

	No. of Treatments	O_2 Consumption/Sq. M./Min.	CO_2 Output/Sq. M./Min.	R. Q.
1. Unmodified electroshock	11	565 ± 136*	540 ± 177*	0.95 ± 0.30*
2. Thiopental	11	347 ± 91* †	305 ± 104* †	0.86 ± 0.13*
3. Succinylcholine-thiopental	10	119 ± 58* ‡	102 ± 59* ‡	0.86 (estimated)

* Standard deviation.
† Significantly different from 1 and 3; $P < 0.01$.
‡ Significantly different from 1 and 2; $P < 0.01$.

resuscitation with succinylcholine. Samples were then taken in the same manner until spontaneous respiration took place and respiratory paralysis was no longer apparent. This technique appeared to provide adequate insurance against errors which might have resulted from retention or excessive elution of carbon dioxide during the period of artificial respiration. In addition, during this period there were no abnormal variations in carbon dioxide concentration of the expired air.

The gas samples thus obtained were then analyzed for volume and for oxygen and carbon dioxide concentration. Those samples collected on patients receiving no drugs, or thiopental alone, were analyzed for oxygen and carbon dioxide with the micro-Scholander apparatus. The samples obtained from the patients receiving succinylcholine-thiopental who received 100% oxygen were analyzed for carbon dioxide on the Haldane gas analysis apparatus. The total volume of expired gas was measured on the Tissot spirometer.

Blood oxygen saturation studies were carried out on a group of patients with the Wood ear oximeter. Readings were taken at 5- to 10-second intervals as long as the values were changing rapidly, and at 10- to 20-second intervals thereafter. Recordings were made until oxygen saturation had returned to pretreatment levels, or until three minutes had elapsed. The findings on 33 treatments were studied. Eleven studies were done on each of three groups of patients receiving electroshock therapy. These were groups receiving unmodified electroshock therapy and electroshock therapy modified by thiopental sodium or succinylcholine and thiopental in combination.

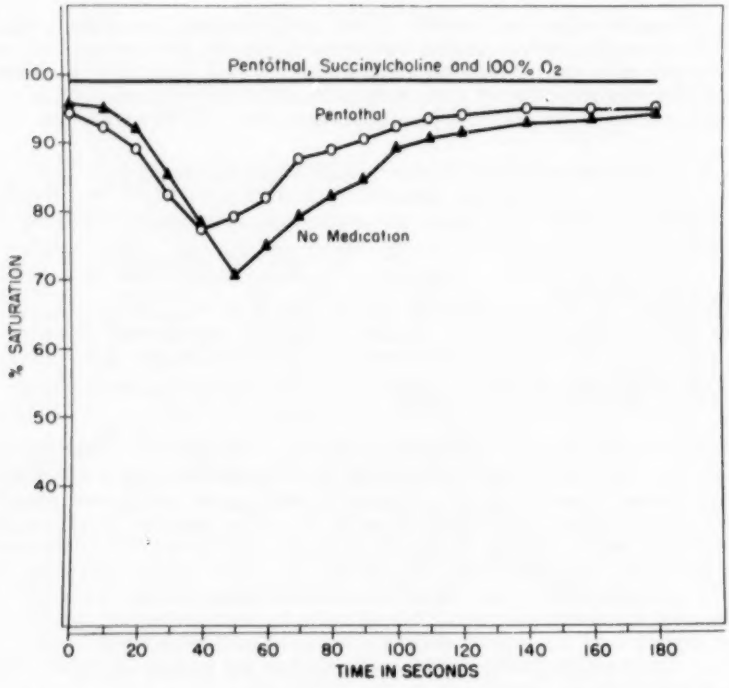
RESULTS

The results of the oxygen consumption studies are summarized in the accompanying Table. The thiopental and succinylcholine-thiopental groups had significantly less oxygen consumption than the control group ($P<0.01$). In addition, the

oxygen consumption of the succinylcholine-thiopental group was significantly below that of the group treated with thiopental alone ($P<0.01$). Because 100% oxygen was used for resuscitation, only carbon dioxide output was measured in the group receiving succinylcholine-thiopental. Oxygen consumption was calculated by using the carbon dioxide output and assuming that the respiratory quotient was the same as that of the group receiving thiopental alone (0.86).

The results of the oxygen saturation studies are summarized in the accompanying Figure. The curves shown are mean curves calculated from results obtained in 11

MEAN ARTERIAL OXYGEN SATURATION CURVES DURING UNMODIFIED AND MODIFIED ELECTROSHOCK



studies in each group. The use of thiopental and succinylcholine-thiopental modifies the oxygen saturation curves. Those patients receiving no premedication show the most marked anoxia and the most prolonged recovery period. Thiopental tends to reduce the severity and duration of anoxia. Succinylcholine-thiopental with 100% oxygen abolishes the anoxia.

COMMENT

The results of this study quantitate previous observations as to the amount of muscular work done during electrically induced seizures. In order to determine the extra amount of oxygen consumed because of the seizure, indirect methods must be used. A physically normal person in a near basal state (fasting, minimal

activity) consumes approximately 150 cc. of oxygen per square meter per minute.[7] By subtracting this figure from the rate of oxygen consumption for the first two and one-half minutes after unmodified electroshock (Table), it is estimated that subjects in the first group contracted an oxygen debt of approximately 1,040 cc. per square meter during the seizure, which had a duration of 30 to 45 seconds. For an average-sized man of 1.73 square meters this would represent a total debt of approximately 1,800 cc. However, because of the short period of collection of samples, averaging only two and one-half minutes, it is probable that only about 70% of the total debt [8] was measured. On addition of remaining 30%, it appears that for unmodified electroshock the total oxygen debt accumulated is approximately 2,600 cc. This debt is equal to about 40% of that acquired by a trained athlete in running the 100-yard dash (6.7 liters).[8] Expressed in other terms, the rate of work in the half-minute after unmodified electroshock (4 to 4.5 liters of oxygen per minute) is similar to the rate at which work is done by a good athlete running the mile race in competition.

Thiopental very markedly alters the oxygen debt. The total oxygen debt contracted is approximately 1,200 cc. of oxygen for the group under thiopental anesthesia. The work rate during seizure corresponds to an oxygen consumption rate of 2,000 cc. per minute. It appears that thiopental reduces by one-half the amount of work done during a seizure. The difference is not based on a different duration of the seizures, since this is approximately the same for unmodified and for thiopental-treated groups.

Arterial oxygen saturation curves are essentially in accord with those reported by Holmberg [6] for unmodified electroshock and electroshock modified with muscle-relaxing drugs. In the present study arterial anoxia was more profound. In some instances values fell to levels of saturation as low as 50%. Anoxia lasted longer in the unmodified group than in the group treated with thiopental. This difference apparently depends upon the great difference in oxygen consumption between the two groups. There were no marked differences between the two groups in the duration of apnea.

The amount of work done after electroshock may be reduced by the use of thiopental or abolished by the use of succinylcholine-thiopental. This knowledge is of clinical value when one wishes to treat patients whose cardiac or pulmonary reserve is limited and who would not be able to tolerate well the effects of severe anoxia, hypercapnia, or excessive activity.

CONCLUSIONS

Thirty-two carbon dioxide excretion studies and 22 oxygen consumption studies were carried out on 28 patients receiving unmodified and modified electroshock therapy. Oxygen saturation curves were obtained on 33 patients.

Anoxia and a markedly increased oxygen consumption are observed in unmodified electroshock. Thiopental used as premedication reduces the anoxia and oxygen consumption. The use of succinylcholine-thiopental reduces oxygen consumption to resting levels. This coupled with the use of 100% oxygen prevents anoxia.

Dr. J. Murdoch and the staff of the State Hospital at Butner, N. C., assisted in carrying out this study.

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PSYCHOLOGICAL STUDIES OF SEVEN EPILEPTIC HEMIPARETICS BEFORE AND AFTER HEMISPHERECTOMY

ALBERT E. UECKER, Ph.D.
CEDAR FALLS, IOWA
LYLE A. FRENCH, M.D.
AND
DAVID R. JOHNSON, M.D.
MINNEAPOLIS

SINCE 1950 there have been a number of reports of the treatment of infantile hemiplegia by hemispherectomy. Cessation of epileptic seizures has been reported in most of these publications, and in some of the cases reported marked improvement in intellectual functioning and personality adjustment has been observed. The results of preoperative and postoperative administrations of psychological tests have been reported, however, in relatively few instances.

During 1952 and 1953 a series of hemispherectomies were performed at the University of Minnesota Hospital. The seven patients were institutionalized epileptics from the State School and Hospital at Cambridge, Minn. The effects of hemispherectomy upon the convulsive disorders, the sensory systems, and the motor systems of these patients were reported in January, 1954, by Johnson, French, and Peyton,[14] and a further report was made by Zarling, French, and Johnson at the April, 1954, meeting of the American Academy of Neurology. The present report is concerned only with the results of the preoperative and postoperative psychological studies.

REVIEW OF RELATED LITERATURE

Removal of the right cerebral hemisphere for the treatment of tumors was first reported by Dandy [7] in 1928. Unfortunately, three of the first five patients died too soon to permit an adequate evaluation of their postoperative mental status. No obvious impairment of mentality was observed in the other two cases.

In 1933 the removal of the right cerebral hemisphere for an infiltrating glioma was reported by Gardner,[11] who performed this operation on three patients. Gardner reported that two of these patients died of hyperthermia within 36 hours. No marked impairment of speech or mental functioning was observed in the surviving patient. Twenty months after the operation relatives and friends could detect no change in her personality or intellectual abilities. Further details of this case were reported by O'Brien,[24] who found that the patient's postoperative memory for recent and past events was good, that she read constantly in spite of her eye difficulty, and that she

Formerly Clinical Psychologist, Cambridge State School and Hospital (Dr. Uecker).
Associate Professor, Division of Neurosurgery, University of Minnesota Medical School (Dr. French).
Research Fellow, National Institutes of Health, United States Public Health Service (Dr. Johnson).

attended well to her household duties. Another instance of the removal of the right cerebral hemisphere was reported by Rowe [26] in 1937. Relatively mild mental changes were observed in this case, and the postoperative results of the Stanford-Binet Intelligence Test were very similar to the preoperative results of the same test. In 1949 Bell and Karnosh [3] reported a relative freedom from gross mental defect in the case of a man who was still living 10 years after hemispherectomy.

A survey of the medical, psychiatric, and psychological literature published between 1928 and 1950 was reported by Mensh, Schwartz, Matarazzo, and Matarazzo [21] in 1952. This survey yielded reports on 41 hemispherectomies, 28 of which were done in the United States. It was found that, with few exceptions, preoperative and postoperative psychological functioning of the patients had been described only in general terms. In the same publication the authors reported the removal of the entire right hemisphere of a 54-year-old man who was suffering from an extensive brain tumor. The Wechsler Memory Scale [28] and various subtests of the Wechsler-Bellevue Intelligence Scale [29] were administered nine times during the five months following surgery. The Rorschach test * was administered three months after the operation. "Wide variations in functioning, with concreteness and perseveration of ideas, confused and psychotic-like thinking, clang associations, mingling of old and new information, and self-reference" were reported. "Premorbid levels of superior vocabulary and verbal facility and extremely compulsive behavior" were also observed. These authors stressed the need for a more systematic follow-up study of the psychological functioning of patients after hemispherectomy.

Successful treatment of infantile hemiplegia and epilepsy by hemispherectomy was reported by Krynauw † in 1950. Hemispherectomies were performed in 12 cases of infantile hemiplegia at the Johannesburg General Hospital, Johannesburg, South Africa. In 10 of these cases the patients were epileptic, and in all of these epileptic cases the epileptic manifestations ceased after operation, without sedative medication. "Marked improvement in personality, behavior, and mentality" was observed in all of the 11 patients that survived operation. In a footnote added after his report went to press, Krynauw [17] stated that eight more patients had been operated upon and that they were making "satisfactory progress."

Another case of an epileptic hemiplegic treated by hemispherectomy was reported in 1950 by Obrador and Larramendi,[23] who stated: "There have been no attacks in the three months since operation. The patient feels quite well and alert. Her previous irritability and aggressive tendencies have completely disappeared. Mental tests show a postoperative improvement in memory."

Preoperative and postoperative psychometric studies of three hemiplegic patients treated by hemispherectomy were reported in 1951 by Davidson.[8] The results of Davidson's testing were in agreement with the observations of Cairns [5] in that they indicated marked improvement in the intellectual functioning of all three patients. Improved social adjustment in all three cases was reported by both Cairns and Davidson.

During the biennium of 1952 to 1953 the successful treatment of intractable seizures by hemispherectomy was reported by several other authors.‡ Of the eight cases that were reported in 1952 by Laine, Fontan, Delandtsheer, and Desfontaines,[18]

* References 2 and 15.

† References 16 and 17.

‡ References 6, 10, 18, 19, 20, 22, and 25.

four were studied intensively for a period of 11 to 12 months, and "diverse variations" were observed in their postoperative mental states; the postoperative intelligence test scores in two of these cases were reported, but no preoperative test scores were reported. Improved personality and, in some cases, improved learning ability were observed in the 18 cases that were reported in 1953 by Cobb and Pampiglione.[6] No change in the mental status was observed in the case of hemispherectomy that was reported in 1953 by Mason and Shapiro.[20]

Although a number of publications since 1950 have reported improvement in personality and intelligence, as well as cessation of seizures following hemispherectomy, the results of preoperative and postoperative psychological examinations by objective methods have been reported in relatively few instances. The present report is concerned with an attempt at objective evaluation of intellectual and other behavioral changes following hemispherectomy for intractable seizures of hemiplegics.

CHARACTERISTICS AND DIAGNOSES OF THE PATIENTS STUDIED

The three male subjects and the four female subjects of this study were selected from the population of the Cambridge State School and Hospital on the basis of having a hemiparesis present from infancy or early childhood which was accompanied, at the time of selection, by epileptic seizures that had responded very poorly to what is generally considered to be adequate dosage of anticonvulsant medication. The diagnosis of birth injuries had been made in four of these cases, of meningoencephalitis in two cases, and of Sturge-Weber syndrome in the remaining case. Preoperatively, evidence of gross pathology of the affected hemisphere was manifested not only by hemiparesis and seizures but also by neurological examinations, electroencephalograms, pneumoencephalograms, and carotid angiograms. The preoperative EEG's showed a severe, diffuse dysrhythmia, usually more pronounced on the affected side.[14]

These patients had been institutionalized for periods varying from 6 to 17 years. At the time of hemispherectomy they ranged in age from 13 to 35 years; in intelligence, they ranged from idiocy to low-normal intellect. Other traits of personality will be discussed in the individual case reports that follow.

NATURE AND EXTENT OF THE OPERATIONS

In all but two of the cases it was the right hemisphere that was removed. The extent of the hemispherectomy varied slightly from case to case, but in general the entire cerebral cortex, including the insula, hippocampal gyrus, and inferior medial orbital gyri, was removed. The depth of the cut was across the internal capsule and included the greater part of the basal ganglia. In the later cases the caudate nucleus was also removed.[14]

PSYCHOLOGICAL TESTS AND METHODS

Because of the heterogeneity of the intelligences studied, it was not feasible to use exactly the same battery of tests for all of the subjects. However, the Stanford-Binet Scale,[27] or the Wechsler-Bellevue Scale[29] or both were administered prior to surgery to all subjects except one, who was entirely mute. The Goodenough Draw-a-Man Test[12] was administered to the younger and duller subjects; the Bender Visual Motor Gestalt Test[4] and the Rorschach Test§

§ References 2 and 15.

were included in the battery for the three adult subjects. Certain other psychological tests, such as the Arthur Point Scale,[1] the Wechsler Memory Scale,[28] the Wechsler Intelligence Scale for Children,[30] and the Minnesota Multiphasic Personality Inventory,[12] were administered in individual cases. A rating of each patient's institutional adjustment was obtained by means of the Vineland Social Maturity Scale.[9] Psychiatric aides were interviewed in order to obtain these ratings; teachers and recreation workers were consulted before the final scoring of some of the items of the Vineland Scale.

Each patient was retested shortly after being returned to the Cambridge institution,‖ and the adjustment of each was rated again by means of the Vineland Social Maturity Scale. The effects of practice on the intelligence tests were minimized by the use of alternate forms or by delayed

TABLE 1.—*Intelligence Quotients of Epileptic Hemiplegics Before and After Treatment by Hemispherectomy*

Case No.	Chron. Age *	Intelligence Scale Used	Before Surgery	After Surgery	After Surgery
1	34	Stanford-Binet	38	38 (17 mo.)	37 (21 mo.)
2	13	Arthur Point Scale	?	20 — (16 mo.)	20 — (21 mo.)
3	19	Stanford-Binet	17	19 (8 mo.)	18 (12 mo.)
4	13	Stanford-Binet	19	16 (7 mo.)	16 (17 mo.)
5	35	Stanford-Binet	70	74 (9 mo.)	76 (12 mo.)
6	30	Wechsler-Bellevue	86	84 (6 mo.)	88 (11 mo.)
7	15	Stanford-Binet	39	42 (1 mo.)	38 (5 mo.)

* Chronological age at the time of hemispherectomy.

TABLE 2.—*Hospital Adjustment (Social Quotients) of Subjects as Measured by the Vineland Social Maturity Scale*

Case No.	Chron. Age *	Preoperative Adjustment	Postoperative Adjustment	Postoperative Adjustment
1	34	22	23 (12 mo.)	23 (21 mo.)
2	13	15	15 (12 mo.)	15 (21 mo.)
3	19	15	10 — (12 mo.)	Died
4	13	32	32 (9 mo.)	38 (17 mo.)
5	35	47	45 (9 mo.)	50 (12 mo.)
6	30	72	72 (8 mo.)	72 (11 mo.)
7	15	52	49 (5 mo.)	52 (6 mo.)

* Chronological age at the time of hemispherectomy.

retesting with identical forms. In April, 1954, all of the subjects were tested and rated once more, except one who had died 13 months after surgery.

RESULTS OF PSYCHOLOGICAL STUDIES

The subjects' intelligence quotients prior to surgery, their intelligence quotients following surgery, and the quotients obtained from a follow-up examination are presented in Table 1. No preoperative I. Q. was obtained for Case 2; several nonverbal tests were attempted, but the patient was too frightened to cooperate. The approximate time interval between the date of hemispherectomy and the administration of the postoperative tests is indicated in parentheses after each of the postoperative test scores.

In general, the postoperative results of intelligence tests were not markedly different from the preoperative results. Some improvement in the intellectual function-

‖ Additional tests were administered to some of the subjects at the Anoka State Hospital by Miss Barbara Rabkin, psychologist. The results of these tests are included in this report.

ing of the two most intelligent subjects (Cases 5 and 6) was indicated by other tests. Further details of this improvement will be given in the individual case reports that follow.

Ratings of the subjects' hospital adjustment prior to surgery, ratings of their adjustment obtained shortly after their return to the Cambridge State School and Hospital, and final ratings, obtained in April, 1954, are presented in Table 2. The approximate time interval between the date of surgery and the dates of the postoperative administrations of the Vineland Social Maturity Scale is indicated in parentheses after each postoperative rating.

The social quotients of the three adult subjects are not directly comparable to their intelligence quotients because of the higher maximum chronological age used in computing the former. The adjustment of these patients tends to be limited by their physical and mental handicaps, even when their seizures are relieved. The adjustment of the more intelligent subjects is limited, also, by institutional routine, which does not provide the opportunities for certain social adjustments that are measured by the Vineland Social Maturity Scale.

Because of the small number of cases studied, statistical treatment of the results was not attempted at this time. Instead, each case was studied individually, and the results are presented below. Chronological ages are listed as attained at the time of surgery.

REPORT OF CASES

CASE 1 (woman, age 34).—There was no marked change either in the intelligence quotients, reported in Table 1, or in the social quotients, reported in Table 2. There were moderate changes in the postoperative results of the Wechsler-Bellevue Scale. Prior to surgery an I. Q. of 46 was obtained with Form II of this scale; 10 months after surgery an I. Q. of 52 was obtained with the alternate form; approximately 2 years after surgery a slightly lower I. Q. was obtained with Form II of the Wechsler Scale. The discrepancy between the results of the Wechsler Scale and those obtained with the Stanford-Binet Scale was primarily a function of the correction for age in the Wechsler norms. The Goodenough Draw-a-Man Test was included in each examination of this subject, and a mental age of approximately 9 years was obtained each time. Qualitative differences were observed in the patient's postoperative performance on the Goodenough test that suggested some impairment in the perception of spacial or part-whole relationships. The patient drew all of the facial features before drawing the outline of the head itself; this resulted in disproportionately large heads in the postoperative drawings.

Some improvement was observed in the patient's postoperative reproductions of the Bender figures; there was no longer a tendency toward perseveration in successive drawings, and fewer figures were badly distorted. There was little change in her postoperative responses to the Rorschach test, but her responses were too meager and too stereotyped to give an adequate basis for judgment. This woman is reported to be less irritable and aggressive than she was before surgery.

CASE 2 (girl, age 13).—Because of the patient's lack of speech, conventional tests of intelligence could not be used. Two nonverbal tests were attempted prior to surgery, but the patient was too dull or too frightened to respond. The Arthur Point Scale and the Goodenough Draw-a-Man Test were administered twice after surgery, and an I. Q. of not more than 20 was estimated from the results. Some improvement in adjustment was revealed by repeated interviews with psychiatric aides. It was reported that the girl was less subject to temper tantrums and that her toilet habits had improved to the extent that she was no longer incontinent. This improved adjustment was barely sufficient to offset the increase in chronological age. Consequently, her social quotient, as measured by the Vineland Social Maturity Scale, did not improve.

CASE 3 (woman, age 19).—No significant change in intelligence was indicated by the I. Q., of 19, that was obtained shortly after surgery with the Stanford-Binet Scale, or by the I. Q. of 18 that was obtained with the alternate form one year after surgery. Prior to surgery a mental

age of less than 3 years was indicated by the Goodenough Draw-a-Man Test; similar results were obtained with this test after surgery. The poorer results obtained after surgery with the Vineland Social Maturity Scale (Table 2) were due largely to aggravation of the patient's physical disability. Some deterioration in personality was suggested by reports of psychiatric aides concerning the patient's postoperative negligence in reporting her need to urinate. The patient died approximately 13 months after hemispherectomy.

Case 4 (boy, age 13).—When this boy was first tested, at the age of 10 years, a mental age of less than 3 years and an I. Q. of 25 was obtained. No further mental development was indicated by the mental age of approximately 2½ years and the I. Q. of 19 that were obtained, prior to surgery, with Form M of the Stanford-Binet Scale. The alternate form of this test was administered 7 months after hemispherectomy, and Form M was readministered 18 months after surgery. An I. Q. of 16 was obtained in both the postoperative examinations. An I. Q. of less than 20 was indicated by the mere scribbling obtained in all three administrations of the Goodenough Draw-a-Man Test. This boy's adjustment, as measured by the Vineland Social Maturity Scale, was better than what might have been predicted from his I. Q. alone; some improvement in adjustment was indicated by the results of the final administration of the Vineland Scale.

Case 5 (woman, age 35).—Six weeks after hemispherectomy an I. Q. of 78 was obtained with the Wechsler-Bellevue Verbal Scale; when uncorrected for age, this score does not differ significantly from the preoperative results of the Stanford-Binet Scale. A slight improvement in intellectual functioning was indicated by the postoperative administrations of the Stanford-Binet Scale (Table 1) and by concurrent administrations of the Wechsler Verbal Scale and the

Intelligence Scale Used	Before Surgery	Six Mo. After Surgery	Eleven Mo. After Surgery
Wechsler-Bellevue (Verbal)	94	98	93
Wechsler-Bellevue (Performance)	77	71	83
Wechsler-Bellevue (Full Scale)	85	84	88
Wechsler Memory Scale (M. Q.)	86	92	108

Arthur Point Scale, a nonverbal test of intelligence. The I. Q. that was obtained with the Arthur Point Scale nine months after surgery was 6 points higher than the preoperative results of this test, and an I. Q. of 82 was yielded by the Wechsler Verbal Scale at this time; very similar results were obtained with these two tests in the final retesting of April, 1954. Some improvement was noted in the patient's postoperative reproductions of the Bender figures; fewer figures were markedly distorted, and there was less tendency toward perseveration in successive drawings.

Improvement in intellectual functioning, or personality adjustment, or both, was indicated by the patient's postoperative responses to the Rorschach test. Prior to surgery she gave only 28 responses to this test. Nine months after surgery, she gave nine more responses, her reaction time was faster, she gave proportionately more "good form" responses, and the content of her responses was somewhat more varied. Little change in institutional adjustment was indicated, however, by the results of the postoperative administrations of the Vineland Social Maturity Scale.

Case 6 (man, age 30).—This subject's scores on preoperative and postoperative tests of intelligence are listed in the accompanying tabulation.

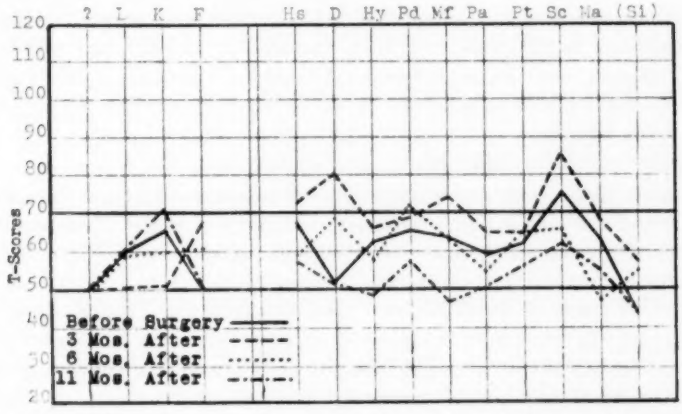
Consistent improvement is evident in the postoperative results of the Wechsler Memory Scale; the other changes were small and variable. The profiles obtained in four administrations of the Minnesota Multiphasic Personality Inventory are shown in the accompanying figure. Although the profile that was obtained three months after surgery was considerably more elevated than the preoperative profile, some improvement in personality was indicated by the second and third postoperative profiles.

Except for the T-score of 75 on the "Sc" scale, all of the preoperative scores on the Minnesota Multiphasic Personality Inventory were within the normal range. This score was even higher in the first postoperative profile, and it was accompanied by an elevated score on the D scale.

Evidently, the patient became depressed, as well as schizoid, during his early convalescence. He gave fewer responses to the Rorschach test and his reaction time was slower, but no intellectual change was indicated by the I. Q. of 97 that was obtained with the Wechsler Verbal Scale at this time. Except for a higher proportion of "good form" responses, the results of the Rorschach test six months after surgery were quite comparable to the preoperative results. Relatively normal profiles were obtained in the last two administrations of the Minnesota Multiphasic Personality Inventory. No marked change in institutional adjustment was indicated, however, by the results of the postoperative administrations of the Vineland Social Maturity Scale.

CASE 7 (boy, age 15).—The mental age of approximately 6 years that was indicated by the preoperative administration of the Stanford-Binet Scale was only one year greater than the mental age that was indicated by the first administration of this test when the patient was 7 years old. No marked change in intelligence was indicated by the I. Q. of 42 that was obtained one month after hemispherectomy with the Stanford-Binet Scale, or by the I. Q. of 38 that was obtained five months after surgery with the alternate form of this test.

Qualitative differences were observed in the postoperative results of the Wechsler Intelligence Scale for Children and the Goodenough Draw-a-Man Test, but there was no significant change in the intelligence quotients that were obtained with these two tests. Subsequent to hemi-



Minnesota Multiphasic Personality Inventory Profiles of Case 6 Before and After Surgery.

spherectomy this patient scored considerably lower on the Performance Scale of the Wechsler test, but he scored somewhat higher at this time on the Verbal Scale. Consequently, his Full-Scale I. Q. remained relatively unchanged.

Although this boy's teacher reports that he is less hyperactive than he was before hemispherectomy, no marked change in institutional adjustment was indicated by the postoperative results of the Vineland Social Maturity Scale (Table 2). A social age of approximately 8 years was indicated by all three administrations of this scale. This boy's institutional adjustment has been better than might have been predicted from his I. Q. alone, but his school progress has been consistent with the results of intelligence tests. He has never progressed beyond primary work, and further achievement can hardly be predicted from the results of the postoperative administrations of the Stanford-Binet Scale.

COMMENT

Although several of the seven subjects of this study seemed somewhat more alert after hemispherectomy, relatively little change in intellectual functioning was indicated by the results of the postoperative administrations of intelligence tests. A slight improvement in intellectual functioning is probable in the two cases of

relatively normal intelligence (Cases 5 and 6). The improvement shown by the latter in his postoperative performance on the Wechsler Memory Scale is comparable to the results of the first case of hemispherectomy that was reported by Obrador and Larramendi.[23]

Except for their freedom from seizures, the postoperative institutional adjustment of these patients is not dramatically different from their preoperative adjustment. Some improvement in adjustment has been observed, however, in at least five of these patients, and in three of the cases (Cases 4, 5, and 6) the postoperative improvement was confirmed by one or more psychometric techniques. Two of the patients (Cases 1 and 2) who were formerly subject to temper tantrums are no longer subject to such tantrums.

In discussing the improvement in intellectual functioning that was shown by her psychometric studies of three hemiplegic patients treated by hemispherectomy, Davidson [8] pointed out that the practice effects of repeated testing and the postoperative reduction or withdrawal of sedative medication might have contributed to the improvement in the patients' scores on intelligence tests. Practice effects were minimized in the present study by the use of alternate test forms and by delayed retesting with identical forms. Although anticonvulsant medication was completely discontinued in only two of the seven cases studied, reduction of the dosage might have contributed to the improvement shown by two of the patients in their postoperative performance on one or more mental tests.

Krynauw,[17] in his interpretation of the improvement observed in the intelligence and adjustment of his patients, assumed the integrity of the remaining cerebral hemisphere. Because of the extremely low intelligence of five of the seven subjects of the present study, it can hardly be assumed that the pathology was entirely limited, in all cases, to the hemisphere that was removed. One of these patients (Case 2) has remained completely mute; it is unlikely that her dominant hemisphere was organically intact. The integrity of the remaining cerebral hemisphere can probably be assumed in the two most intelligent patients (Cases 5 and 6), and in these two cases some improvement in intellectual functioning was indicated by the postoperative tests.

SUMMARY

Seven cases of infantile hemiplegia were given psychological examinations before and after hemispherectomy. Improved adjustment was indicated in at least five of these cases by psychometric techniques or by interviews with psychiatric aids. Intellectually, none of these patients fell below the preoperative level, and some improvement in mental functioning is probable in two of these cases, although it is possible that this improvement is an artifact due to the reduction or withdrawal of drugs.

Although hemispherectomy has proved to be a rather effective treatment for the convulsions and personality disorders that are often associated with infantile hemiplegia, improvement in intellectual functioning does not always occur. Improvement in mental functioning is probably dependent upon the integrity of the remaining hemisphere, which can hardly be assumed in cases of idiocy or imbecility. Further research by means of objective psychological techniques will be necessary before hemispherectomy can be recommended as a means of improving the intellectual functioning of hemiplegics.

This study has been made possible through the cooperation of Dr. Raymond Gully, Superintendent of the Cambridge State School and Hospital; Dr. John Reitman, Superintendent of the Anoka State Hospital, and Dr. Ralph Rossen, Superintendent of the Hastings State Hospital. Dr. Zondal Miller, Consultant in Neurology to the Anoka State Hospital, has examined all of the patients preoperatively and, in addition, did the encephalograms and angiograms. Several of the patients were given psychological tests at the Anoka State Hospital by Miss Barbara Rabkin, psychologist. Accurate appraisal of the preoperative and postoperative adjustments of the subjects of this study would have been impossible without the cooperation of psychiatric aides, teachers, and recreation workers, whose intimate acquaintance with the patients enabled them to furnish many essential data. Mr. Jarle Leirfallom, Director of Public Welfare, State of Minnesota, made funds available so that these patients could be transferred for treatment.

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PROGNOSIS IN TRANSORBITAL LOBOTOMIES RELATIVE TO BODY TYPE

NATHAN S. KLINE, M.A., M.D.
ASHTON M. TENNEY, M.A., M.S.
ORANGEBURG, N. Y.
FRANK S. DIMON, M.S.W.
AND
WILBUR M. LUTZ, M.D.
WERNERSVILLE, PA.

THE ESTABLISHMENT of a relationship between body type and response to psychosurgical procedures not only would be of theoretical interest but could be of use in selecting patients with a prognosis favorable enough to warrant the operative risk. The finding of such a correlation would not be demonstration that body type determined or "caused" the particular response but would only indicate that it was measurably related to such factors as did determine the result and might therefore be of prognostic value. In previous studies * it has been demonstrated that such a relationship probably exists, and the results in the series of 102 patients who received transorbital lobotomies tend to confirm this impression.

Patients from the Wernersville State Hospital, Wernersville, Pa., were operated on in late 1949 and early 1950. They were photographed in October, 1951, and the present article covers the period until January, 1953, so that the postoperative period is three years. As in previous series, the somatotype ratings of the medical photographs were made by Dr. W. H. Sheldon, who had no information about the patients other than age, height, and weight history.

The original series, as reported by Moore, Hill, and Lutz,[4] was made up of 62 females and 40 males. Since unpublished surveys by one of us indicate that female psychosurgical patients have a poorer prognosis than males, data are considered separately for each sex. The present series omits 9 of the 16 discharged males and 9 of the 17 discharged females because of photographic difficulties or unavailability of the patients. There is no way of knowing the body type of these missing patients, which factor is indicative of the need for planning such research in advance.

RESULTS

As in the unpublished series, the discharge rate of the females was less than that of the males. At the end of the three-year period 40% of the males were out

Clinical Director, Wernersville State Hospital (Dr. Lutz).
Chief, Social Service, Wernersville State Hospital (Mr. Dimon).
Senior Research Scientist, Research Facility, Rockland State Hospital (Mr. Tenney).
Director, Research Facility, Rockland State Hospital, Orangeburg, and Department of Neurology, Columbia University College of Physicians and Surgeons, New York (Dr. Kline).

* References 1, 2, and 3.

of the hospital, as opposed to 27.4% of the females. One cannot conclude from this that the operation is routinely more successful on one sex than on the other, because there may have been different relevant factors determining the selection of the male or female patients for operation. Comparisons should be made only between patients within the series, since selection for the series was not controlled.[5]

In a previous series of psychosurgical male patients, the mesomorphs were found to have a relatively good prognosis and the endomorphs to have poor expectation of discharge.[2] In the present series, of 31 somatotyped males, 30% of the endomorphs, 45% of the mesomorphs, and 33% of the ectomorphs had been discharged at the time of this study. The total number of cases is small, but the trend is definite.

The group of 53 somatotyped women provided our first real psychosurgical series of females. We find that females (who are normally much more endomorphic than the males) have a significantly poorer prognosis if their endomorphy is below

Summary of Data on Eighty-Four Somatotyped Patients, Three Years Postoperatively

	Discharged	Hospitalized
Sex *		
Male	16 (40%)	24 (60%)
Female	17 (27%)	45 (73%)
Total Endowment		
Above average	14 (35%)	26 (65%)
Below average	8 (18%)	36 (82%)
Males		
Mesomorphic	5 (45%)	6 (55%)
Nonmesomorphic	5 (25%)	15 (75%)
Females		
Above average endomorphy	9 (35½%)	15 (62½%)
Below average endomorphy	3 (10%)	26 (90%)

* Data on total group of 102 patients rather than on only the 84 somatotyped.

the mean for the total group. The group of women had an average endomorphy of 47%. Of those with less than average endomorphy, only 10% were discharged (3 of 29), in contrast to 37.5% (9 of 24) for those with more than average endomorphy. This is statistically significant at better than the 1% level.

One other factor emerges as being of considerable interest. The sum of the somatotype ratings is designated as the "total endowment," e. g., a 3-3-3 would have a total endowment of 9, and a 4-4-4, one of 12. In the present series both male and female patients with greater than average endowment (11 or above for males, and 10½ or above for females) tended to have a better prognosis. Only 18% of the total group with below-average total endowment were discharged, in contrast to 35% of the above-average group.

COMMENT

Evidence continues to accumulate that gross morphology is relatable to prognosis, particularly in response to psychosurgical procedures. An extensive series, photographed in advance, should provide valuable data as to who are the patients most likely to respond favorably to such operations.

SUMMARY

In a series of 84 somatotyped patients with transorbital lobotomies, (*a*) mesomorphic males and (*b*) females with above-average endomorphy gave the best response.

The percentage of females discharged was smaller than that of males.

Patients with above-average total endowment did better than those with total endowment below the average.

A more extensive study relating somatotype to response to psychosurgery would be of value in selecting candidates for this procedure.

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BRAIN TUMOR AND LUMBAR PUNCTURE

LOWELL G. LUBIC, M.D.
PITTSBURGH
AND
JOSEPH T. MAROTTA, M.D.
NEW YORK

A NUMBER of observers have reported untoward reactions following lumbar puncture in patients with tumors of the brain or with increased intracranial pressure due to other causes.* These untoward reactions have been attributed to temporal lobe herniation or herniation of the cerebellar tonsils. In some of the cases death is reported to have occurred immediately from presumed compression of vital centers, and in others a train of symptoms have developed which are presumed to indicate a more gradual compression.

The statement is frequently seen that lumbar puncture is dangerous and is contraindicated whenever papilledema is present. This conclusion is reached on the basis of untoward reactions in individual cases, and to our knowledge there has not been an analysis of the results in a large series of cases. This study was undertaken in order to determine the frequency of untoward reactions in a large series of patients with tumors of the brain on whom a lumbar puncture was performed.

MATERIAL

All of the available brain tumor cases (965) at the Neurological Institute of New York, from January, 1945, to July, 1953, were reviewed; only those patients who had lumbar puncture performed prior to arteriography, air studies, or surgery were included. A total of 401 histologically verified cases were available for this study, with the exception of 15 brain stem neoplasms that were verified by surgery or air studies.

For this survey, the status of all the patients was carefully evaluated from the time of the lumbar puncture until arteriography, air studies, or surgery. A careful search was made for the presence of symptoms or signs indicating an adverse effect of the lumbar puncture, with special attention to signs of temporal lobe herniation or herniation of the cerebellar tonsils. Particular attention was given to the following: third nerve involvement as evidenced by pupillary dilatation or extraocular muscle paralysis; changes of the blood pressure, pulse, respirations, and temperature; the appearance of convulsions; decerebrate rigidity; changes in the state of consciousness, and unexpected progression in neurologic deficit.

RESULTS

Division of the cases according to the anatomical location and histologic type is shown in Table 1. There were 164 tumors in the anterior fossa, 140 in the middle fossa, 74 in the posterior fossa, 10 in the sellar and parasellar region, and 13 multiple metastatic lesions. The general histologic distribution of these cases followed that reported in other large series of cases of brain tumors.

From the Neurological Institute of the Presbyterian Hospital, New York.

* References 1 through 5.

According to most observers, herniations through the foramen magnum and tentorial notch are most apt to occur when there are mass lesions in the posterior fossa or temporal lobe. There was a total of 74 mass lesions of the posterior fossa in this series. Of these cases, 12 had obvious papilledema, 17 had questionable papilledema, and 44 had normal optic discs (Table 2). A total of 29 cases showed evidence of increased intracranial pressure by lumbar puncture. There were no patients in this particular group that showed any untoward symptoms or signs following lumbar puncture.

There were 140 cases with middle fossa neoplasms; of these, 57 were present in the temporal lobe. One case showed symptoms and signs possibly indicating uncal herniation following lumbar puncture. A detailed description of this case is presented below:

O. H., #975865.—This 62-year-old white woman was admitted to another hospital on Nov. 9, 1949, for a lumbar puncture. No neurologic examination was performed. An initial pressure of 300 mm. of cerebrospinal fluid was recorded during lumbar puncture; the amount of fluid removed was not recorded. The patient had no untoward effects immediately after this procedure. Twelve hours later, on Nov. 10, while preparing to be discharged, she developed a severe occipital headache and became stuporous. On examination, the left pupil was slightly larger than the right, but both pupils reacted well to light; there was bilateral papilledema with hemorrhages. There was a flaccid paralysis of the left arm, but the other extremities could be moved; sensation was grossly intact, and the abdominal reflexes were absent. There was a preponderance of the deep tendon reflexes in the right leg. The plantar responses were normal. The patient was transferred to the Neurological Institute of New York on Nov. 12. The blood pressure was 150/90, pulse rate 72 per minute, and temperature 99 F. per rectum. The patient was stuporous and appeared to be having considerable pain over the back of her neck. The left arm was spastic and the left leg flaccid. The deep tendon reflexes were more active on the left side than on the right. There were no pathological reflexes. The cranial nerves appeared normal except for bilateral papilledema with hemorrhages; the pupils were dilated and reacted sluggishly to light; the left pupil was slightly larger than the right, and there was marked nuchal rigidity. Sensation to pin was intact.

A ventriculogram outlined a right temporal lobe mass lesion. After this procedure a biopsy was performed through a right temporal burr hole. The pathologic diagnosis was glioblastoma multiforme. The patient never regained consciousness and died 48 hours after admission. Permission for autopsy was not granted.

In the remainder of the patients with lesions in the anterior fossa, multiple metastatic lesions, and sellar and parasellar lesions, there were no changes following the lumbar puncture. Each of the multiple metastatic tumors had at least one lesion in the posterior fossa.

The optic fundi in all cases were seen by at least two neurologists. In addition, the abnormal ones were seen by an ophthalmologist. For the purpose of simplicity the cases were divided into patients whose fundi showed obvious papilledema, patients with questionable papilledema, and patients with normal-appearing fundi. In the anterior fossa there were 19 cases of obvious papilledema and 32 of questionable papilledema; in the middle fossa, 14 of obvious papilledema and 26 of questionable papilledema; in the posterior fossa, 12 of obvious papilledema and 17 of questionable papilledema; in the multiple metastatic group, 4 of questionable papilledema and 1 of obvious papilledema, and in the sellar and parasellar lesions, none showed any evidence of papilledema. Thus there were 46 (12%) cases of obvious papilledema and 79 (20%) cases of questionable papilledema in this series (Table 2).

TABLE 1.—*Location and Types of Brain Tumor in 401 Patients*

Anterior fossa, 164 (41%)	
Glioblastoma multiforme	67
Astrocytoma	43
Meningioma	24
Metastatic tumors	17
Oligodendroglioma	10
Miscellaneous tumors	3
Posterior fossa, 74 (18.5%)	
Meningioma	16
Brain stem (intrinsic)	15
Metastatic tumors	13
Astrocytoma	9
Acoustic neurinoma	7
Hemangioblastoma	7
Miscellaneous tumors	4
Medulloblastoma	3
Middle fossa, 140 (35%)	
Glioblastoma multiforme	68
Metastatic tumors	24
Astrocytoma	19
Meningioma	19
Oligodendroglioma	6
Miscellaneous tumors	4
Sellar and parasellar region, 10 (2.5%)	
Pituitary adenoma	3
Craniopharyngioma	2
Chordoma	2
Glioma of optic chiasm	2
Pinealoma	1
Multiple metastatic lesions, 13 (3%)	

TABLE 2.—*Relation of Location and Type of Brain Tumor to the Optic Discs*

Location of Tumor	Obvious Papilledema	Questionable Papilledema	Normal Fundi	Not Seen
Anterior fossa, 164 (41%)				
Glioblastoma multiforme	7	11	47	2
Astrocytoma	7	11	25	0
Meningioma	2	3	18	1
Metastatic tumor	3	4	11	0
Oligodendroglioma	0	2	8	0
Miscellaneous tumors	1	1	1	0
Total	19	32	110	3
Middle fossa, 140 (35%)				
Glioblastoma multiforme	6	14	48	0
Metastatic tumor	3	5	15	1
Astrocytoma	1	3	15	0
Meningioma	2	1	16	0
Oligodendroglioma	1	2	3	0
Miscellaneous tumors	1	1	2	0
Total	14	26	99	1
Posterior fossa, 74 (18.5%)				
Meningioma	3	2	10	1
Brain stem (intrinsic)	1	3	11	0
Metastatic tumor	1	4	8	0
Astrocytoma	4	2	3	0
Acoustic neurinoma	1	3	3	0
Hemangioblastoma	0	3	4	0
Miscellaneous tumors	0	0	4	0
Medulloblastoma	2	0	1	0
Total	12	17	44	1
Sellar and parasellar region, 10 (2.5%)				
Pituitary adenoma	0	0	3	0
Craniopharyngioma	0	0	2	0
Chordoma	0	0	2	0
Glioma optic chiasm	0	0	2	0
Pinealoma	0	0	1	0
Total	0	0	10	0
Multiple metastatic lesions, 13 (3%)	1	4	8	0
Total	1	4	8	0

Papilledema can be caused by lesions other than brain tumors and "although it has been regarded as presumptive evidence of increased intracranial pressure due to a mass lesion of the brain, we now know that practically or identically the same appearance of the eye grounds is found in non-surgical lesions, both with and without increased intracranial pressure." [6] Lumbar puncture may aid in a differential diagnosis of papilledema caused by nonmass lesions, such as diabetes mellitus, chronic meningeal infections, hypertension, local vascular lesions of the retina, acute encephalitis, congenital malformation of the optic discs, syphilis, and

TABLE 3.—*Relation of Location and Type of Brain Tumor to Spinal Fluid Pressure*

Location of Tumor	Cerebrospinal Fluid Pressure, Mm. Water *							
	0-100	101-150	151-200	201-250	251-300	301-400	401-Over	N. R.†
Anterior fossa								
Glioblastoma	5	25	17	7	5	4	2	2
Metastatic tumor	2	5	4	1	4	0	0	1
Astrocytoma	1	15	7	8	3	1	3	5
Meningioma	0	3	10	3	1	0	0	7
Oligodendroglioma	2	5	0	0	1	0	0	2
Miscellaneous tumors	1	0	0	0	0	0	0	2
Middle fossa								
Glioblastoma	2	23	13	10	6	6	1	7
Metastatic tumor	4	2	12	3	1	1	1	0
Astrocytoma	2	5	3	4	3	0	0	2
Meningioma	0	6	7	2	1	0	1	2
Oligodendroglioma	1	1	2	1	0	0	0	1
Miscellaneous tumors	1	1	0	1	0	1	0	0
Posterior fossa								
Meningioma	1	4	2	5	2	0	0	2
Brain stem (intrinsic)	4	2	3	1	2	0	0	3
Metastatic tumor	1	0	6	4	0	0	1	1
Astrocytoma	0	1	1	2	1	2	0	2
Acoustic neurinoma	1	1	2	2	1	0	0	0
Hemangioblastoma	0	0	3	1	0	0	1	2
Medulloblastoma	0	1	0	1	0	0	0	1
Miscellaneous tumors	0	1	3	0	0	0	0	0
Sellar and parasellar region	0	2	2	2	1	0	0	2
Multiple metastatic lesions	2	1	3	1	3	1	0	2
Total	30 (7.5%)	104 (26%)	102 (25.5%)	59 (14.7%)	35 (8.7%)	16 (4%)	10 (2.5%)	45 (10.1%)

* When more than one lumbar puncture was performed, an average spinal fluid pressure was recorded.
† Not recorded.

demyelinating diseases.† In these cases the information obtained by lumbar puncture may help avoid unnecessary arteriography, air studies, and surgery.

The 401 patients had a total of 447 lumbar punctures. All the patients were tapped with either a No. 18, 19, or 20 gauge needle. An average of 8 cc. of cerebrospinal fluid was removed, and all pressures were recorded with the patient in the lateral recumbent position. Only pressures of 190 mm. of cerebrospinal fluid, and above, were considered as elevated. In the anterior fossa, there were 44 cases of increased cerebrospinal fluid pressure; in the middle fossa, 47 cases; in the posterior fossa, 29 cases; in the multiple metastatic group, 4 cases, and in the sellar and parasellar lesions, 3 cases. Thus, a total of 127 (32%) cases showed increased pressure

† References 7 through 9.

by lumbar puncture. Of these 127 cases, 33 had obvious papilledema, 40 had questionable papilledema, and 60 had normal optic fundi (Table 3).

In 100 (25%) cases, the diagnosis of neoplasm was substantiated by an elevated cerebrospinal fluid pressure, even though the optic discs showed no obvious papilledema.

SUMMARY

The findings are reviewed in a series of 401 patients with histologically verified brain tumors in whom a lumbar puncture was performed. It is realized that these patients represent a selective group in that lumbar puncture is not routinely performed in patients with brain tumor, and many cases with a high degree of papilledema were not subjected to this test. However, papilledema (32%) and increased cerebrospinal fluid pressure (32%) were present in a significant percentage of the cases. Mass lesions were located in the temporal lobe in 14%, and in the posterior fossa in 18.5%. Only one case showed evidence indicating an untoward effect of the lumbar puncture. Lumbar puncture was of aid in establishing the diagnosis of neoplasm in a large percentage of the cases. It should be emphasized that lumbar puncture should be performed only when the findings will be of aid in establishing the correct diagnosis. It is not indicated when the diagnosis is quite evident from the history, physical examination, and laboratory data.

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PATHOGENESIS OF HEPATOCEREBRAL DISEASE

II. Histochemical Study of Copper of Liver and Brain in Wilson's Disease

SHIGEO OKINAKA
MASAKI YOSHIKAWA
MASATERU TOYODA
TOSHIJI MOZAI
YASUO TOYOKURA
AND
MASAKUNI KAMEYAMA
TOKYO

IN OUR previous paper, on "a case of hepatolenticular degeneration," [1] we reported that we could confirm the definite increase of copper excretion in the urine and could demonstrate that dimercaprol (BAL) treatment gave rise to the marked increase of copper excretion. In this paper we report histochemical findings in the liver and brain in Wilson's disease (hepatolenticular degeneration). Recently, case reports of Wilson's disease are appearing rather frequently in Japan, and we were able to obtain five livers and two brains from autopsy materials of the School of Medicine of Tokyo, Tohoku Imperial University, Osaka University, and Saint Luke's Hospital of Tokyo. Copper granules were demonstrated histochemically in four of these five livers and in the putamen of one brain.

MATERIAL AND METHOD

Livers were obtained at autopsy and fixed in 10% formalin before examination. Histochemical demonstration of copper was performed by the method of Okamoto and Utamura,[2] in which rubeanic acid and *p*-dimethylaminobenzylidenerhodanine are used as reagents. Rubeanic acid is considered to be more specific and sensitive. With the rubeanic acid method copper is demonstrated as green granules against alum-carmine counterstaining, and with the rhodanine method, as red-brown granules against hematoxylin staining. Gomori stated that, contrary to the findings of Okamoto, positive results were never obtained in human tissues by the rubeanic method.[3] However, we observed always the marked parallelism of results with the rubeanic acid and rhodanine methods in the liver in Wilson's disease, and demonstrated that both methods are excellent for the demonstration of copper in human tissue. Fixation in alcohol may be preferable, but materials fixed in 10% formalin gave satisfactory results.

The quantitative determination of copper was performed according to the method of Kimura and Murakami,[4] introduced by us in the previous report.[5] Tissues are ignited by the wet-ashing method with sulfuric and perchloric acid, and copper is isolated from other metals, using dithizone-carbon tetrachloride solution. The separated copper becomes golden-yellow when diethyldithiocarbamate is added. The colored substance is extracted with carbon tetrachloride and is measured colorimetrically.

From the Third Internal Clinic of Prof. S. Okinaka, University of Tokyo School of Medicine.

RESULTS

1. *Copper in the Liver of Wilson's Disease.*—All five cases were of typical Wilson's disease with Kayser-Fleischer ring, extrapyramidal symptoms, and fatal outcome. The livers showed diffuse nodular cirrhosis. The results of quantitative

TABLE 1.—*Copper Content in Wilson's Livers*

Case No.	Copper Content, Mg. per 100 Cc.	Histochemical Finding
1	13.1	—
2	34.8	+
3	32.8	+
4	44.1	+
5	55.5	+

TABLE 2.—*Copper Content in Control Livers*

Case No.	Diagnosis	Sex	Age, Yr.	Copper in Livers	
				Copper Content, Mg. per 100 Cc.	Histochemical Finding
1	Laennec's cirrhosis	F	43	....	—
2	Laennec's cirrhosis	F	50	....	—
3	Laennec's cirrhosis	M	55	14.1	+
4	Laennec's cirrhosis	F	40	8.3	—
5	Laennec's cirrhosis	F	53	2.9	—
6	Laennec's cirrhosis	F	44	....	—
7	Acute yellow atrophy	M	25	....	—
8	Acute yellow atrophy	M	50	1.3	—
9	Acute yellow atrophy	M	50	....	—
10	Acute yellow atrophy	M	26	....	—
11	Subacute yellow atrophy	M	19	14.3	+
12	Biliary cirrhosis	F	65	5.9	—
13	Biliary cirrhosis	F	13	....	—
14	Biliary cirrhosis	M	30	....	—
15	Congestive liver (heart failure)	F	25	....	—
16	Congestive liver (heart failure)	M	52	5.1	—
17	Congestive liver (heart failure)	M	49	4.4	—
18	Liver cancer	M	40	6.3	—
19	Liver cancer	M	39	8.3	—
20	Liver cancer	M	45	8.0	—
21	Banti's syndrome	F	60	6.0	—
22	Banti's syndrome	M	52	....	—
23	Banti's syndrome	F	42	....	—
24	Hodgkin's disease	M	44	....	—
25	Infectious hepatitis	M	53	2.9	—
26	Liver abscess	M	38	....	—
27	Leukemia	M	38	....	—
28	Gastric cancer	M	48	1.7	—
29	Gerstmann's syndrome	F	58	....	—
30	Lung cancer	M	64	....	—
31	Peritonitis carcinomatosa	M	49	....	—
32	Bronze diabetes	M	52	2.2	—
33	Beriberi	M	48	....	—

and histochemical investigation are shown in Table 1. The livers of Wilson's disease contained large amounts of copper in comparison with the controls (Table 2). Histochemically, copper was demonstrated as green (rubeanic acid method) or as red-brown (rhodanine method) granules in the protoplasm of the liver cell. In Kupffer cells no copper was found. In a lobule with a positive copper reaction,

there was no difference in the density of copper granules in the central, intermediate, and peripheral zones. However, while one lobule had dense distribution of copper granules in all liver cells, other lobules contained almost no copper granules.

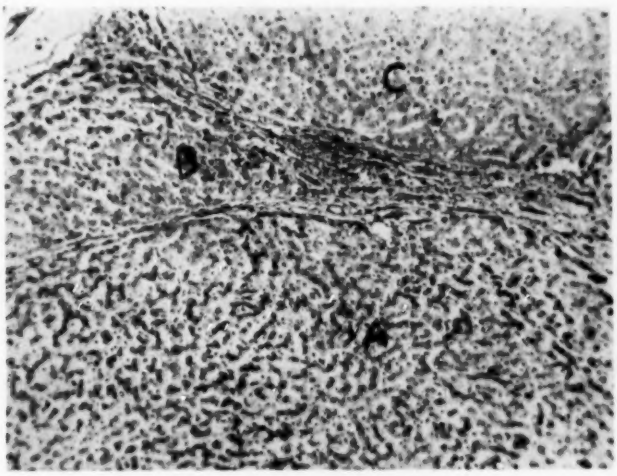

Fig. 1.—Copper granules in the liver of Wilson's disease (rhodanine stain). Lobule *A* contains abundant copper granules, while in lobules *B* and *C* no granules were demonstrated.

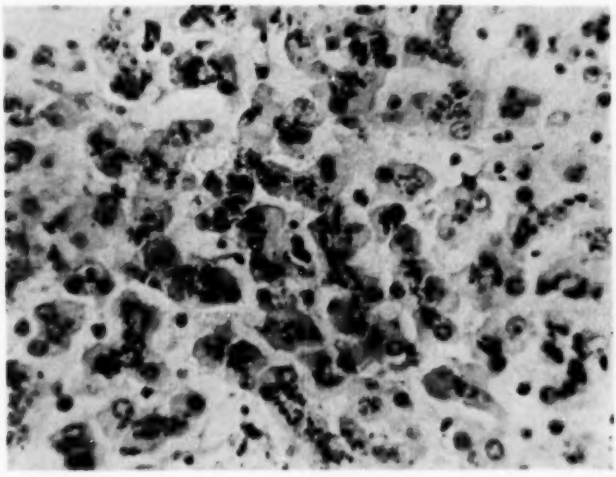

Fig. 2.—Copper granules in the liver of Wilson's disease (rhodanine stain). Copper granules are found exclusively in protoplasm of liver cells.

This difference of copper content among individual lobules has attracted much attention in histochemical findings (Figs. 1 to 3).

2. *Copper in Control Livers.*—As shown in Table 2, the livers in 33 cases were investigated. Included were 6 cases of Laennec's cirrhosis, of which 2 belonged to a

specific type of hepatocerebral disease,[6] 5 cases of acute and subacute yellow atrophy, 3 cases of biliary cirrhosis, 3 cases of congestive liver, 3 cases of Banti's syndrome, and 10 cases of miscellaneous diseases. Of these 33 livers, only 2 showed positive results in copper staining, namely, one with Laennec's cirrhosis and one with subacute yellow atrophy. The amounts of copper in these two livers were 14.1 and 14.3 mg. per 100 cc., respectively, which, though somewhat increased over the normal, are smaller than the amount of copper in the liver in Wilson's disease. The copper granules demonstrated in these two cases were distributed only in the peripheral zone of certain lobules. As in the liver of Wilson's disease, they were demonstrated exclusively in the protoplasm of liver cells and could not be found in Kupffer cells or in the connective tissue cells.

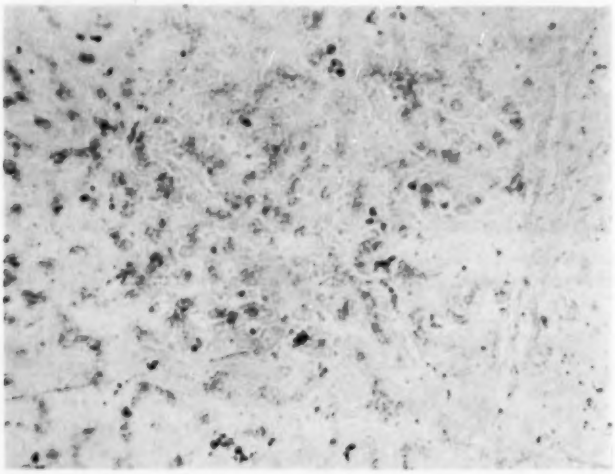

Fig. 3.—Copper granules in the liver of Wilson's disease (rubeanic acid stain).

TABLE 3.—*Copper Content of Gray Matter of Cerebrum in Controls*

Case No.	Diagnosis	Gray Matter of Cerebrum	
		Copper Content, Mg. per 100 Cc.	Histochemical Finding
1	Laennec's cirrhosis	1.5	—
2	Biliary cirrhosis	5.8	—
3	Congestive liver	3.0	—
4	Lung cancer	8.7	—
5	Peritonitis carcinomatosa	8.3	—
6	Diabetes mellitus	4.4	—

TABLE 4.—*Copper Content of Brain in a Case of Wilson's Disease*

Part of Brain	Copper Content, Mg. per 100 Cc.	Histochemical Finding
Putamen	45.8	+
Gray matter of cerebrum	14.3	—
White matter of cerebrum	13.4	—

3. *Copper in Brain.*—The copper contents of the gray matter of the cerebrum in six cases of control diseases are shown in Table 3. The putamen of the brain in the case of Wilson's disease showed the value of 45.8 mg. per 100 cc. (Table 4). Copper granules were demonstrated in this region. Unlike the copper granules in the liver, those in the brain were not found easily. However, on microscopic observation, they were found in the protoplasm of some glia cells. In ganglion cells no copper was demonstrated.

COMMENT

Since the reports of Cumings,[7] Denny-Brown and Porter,[8] Porter,[9] and others, the increased copper content of the urine or the liver of Wilson's disease has been confirmed by several authors. Our experience with Japanese patients corroborated definitely the presence of a disturbance of copper metabolism in Wilson's disease. Furthermore, our histochemical demonstration of copper indicated a specific distribution of copper in liver and nerve tissue. In liver, some lobules had abundant copper granules in all liver cells, while other lobules contained almost no demonstrable copper granules. This finding seems to have some relationship to the functional and morphological peculiarity of the liver of Wilson's disease.

In addition to Wilson's disease, a slight increase in copper content or the presence of a few copper granules in the liver cells was found sometimes in liver cirrhosis or in acute yellow atrophy of the liver. Such findings had already been reported by Okamoto, in 1939.[10] However, the quantitative difference of the copper content between these liver diseases and Wilson's disease is so marked that the presence of copper granules in some hepatic diseases does not change our concept regarding the disturbance of copper metabolism as the special feature of Wilson's disease. This idea was confirmed further by our demonstration of copper granules in the putamen of the brain of a patient with Wilson's disease. Histochemical investigations of copper in the brains of patients with other diseases have all been negative. Our experimental work, in which the livers of dogs, injected with copper solution repeatedly, showed marked increase of copper content and the presence of copper granules, failed also to demonstrate copper granules in the brain. Therefore, it seems to be more difficult or rarer for copper to increase in the brain than in the liver, and the histochemical demonstration of copper granules seems to be the most pathognomonic finding in Wilson's disease. We suspected that Alzheimer's cell, which has been given special attention in the morphological study of the brain in Wilson's disease might have some relation to copper. From the finding of copper granules in the brain of Wilson's disease, it was definitely demonstrated that copper was taken up and contained by glia cells. While some copper-containing glia cells had apparently normal nuclei, others showed swollen, chromatin-poor nuclei. Therefore, it may be possible that Alzheimer glia cells are the remains of these glia cells, whose protoplasm was poisoned by copper and dissolved.

SUMMARY

The copper content of the liver and brain was investigated by histochemical, as well as quantitative, methods in 5 cases of Wilson's disease and in 33 control cases of other diseases. In four of the five livers of Wilson's disease, the copper content was much higher than that of the controls. With the histochemical method, copper granules were demonstrated in the liver of these cases of Wilson's disease.

It was found that some lobules had abundant copper granules in all liver cells, while in other lobules almost no copper granules were demonstrated. Of the 33 control livers, a slight increase of copper was seen only in two. In the putamen of a brain of Wilson's disease, copper granules were demonstrated in the protoplasm of glia cells. The role of copper in the development of Alzheimer's glia cell is discussed.

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INACTIVATION OF ANTIBODIES

A Causative Factor of Brain Pathology in Acute Lead Intoxication

HAROLD W. WILLIAMS, M.D.
WENDELL T. CARAWAY, Ph.D.
WILLIAM A. de YOUNG, M.D.
PROVIDENCE, R. I.

THE CASE of a 23-month-old girl, who died after an acute illness of a week, was studied in this hospital. The interrelationship of somatic disease and the pathological functioning and pathological anatomy of the central nervous system has been a topic of emphasis in the laboratory of neuropathology of this Institute.

There is the principle that the kind, predilection, and distribution of lesions of the central nervous system are to be understood through the subtlety of the interrelation of multiple factors. This idea contrasts with the previous belief in the specificity of changes in the central nervous system. The emphasis on the interrelationship of somatic disease and changes in the functioning and anatomy of the central nervous system has given increasing meaningfulness to this principle.

The neuropathological findings observed in this case seemed most consistent with a pathogenesis of bacterial toxins derived from a bacterial growth in the circulating blood, namely, a septicemia. The history of paint eating, in the abnormal amounts of lead in the blood and feces, pointed to an exogenous toxin, namely, lead, in the pathogenesis of the neuropathological findings. This discrepancy could be understood if certain assumptions were made. Suppose that the abnormal concentration of lead in the blood inactivated antibodies, so that the usual resistance to bacterial invasion and growth were diminished; then brain change could be due to bacterial toxins rather than to lead intoxication.* In vitro experiments indicate that lead does inactivate antibodies and, hence, diminishes body defenses to bacterial invasion and growth.

REPORT OF A CASE

History.—A 23-month-old child, with normal delivery and in good health, who had displayed a two-month pattern of chewing painted objects, suffered an acute illness of nine days' duration. The onset was characterized by vomiting and a temperature of 100 F. Vomiting became spasmodic. The fever continued. Lethargy and closure of the left eyelid gradually appeared. The patient was admitted as a brain tumor suspect to the Neurosurgical Service of Rhode Island Hospital 30 hours before death.

There was lethargy, left-lid ptosis, a "cracked pot" sound, and bilateral papilledema. Convulsive movements of the arms and head appeared 21 hours before death and continued episodically until death. Eight hours before death, the spinal fluid pressure was 400 mm. of water, and the total protein 393 mg. per 100 cc. The blood count was as follows: 7 gm. of hemoglobin per 100 cc.; 5,140,000 red blood cells per cubic millimeter, and 15,250 white blood

From the Institute of Pathology, Rhode Island Hospital.

* References 1 and 2.

cells per cubic millimeter, with 77% polymorphonuclear leucocytes, 15% lymphocytes, and 8% monocytes. Hematocrit level was 33%. No stippling. There was no lead line in the long bones. Skull x-ray was normal. Lead in the feces was 5.68 mg. per 100 cc. Lead in the blood was 0.348 mg. per 100 cc. Throat culture showed Escherichia intermedium and an anaerogenic paracolon bacillus, Type 5W.

Postmortem Findings.—The brain weighed 950 gm. In the gross the brain appeared blanched. The gyri were somewhat flattened and the sulci narrowed. Otherwise, the gross examination was normal. There was congestion and atelectasis of both lower lobes of the lungs. The liver was congested.

Microscopic Findings.—Multiple sections of the brain were stained by the Nissl and Weil methods. There were several areas of "paling" in the white matter † and multiple areas of "paling" in the putamen and the caudate nuclei. A beginning area of "paling" was present in the subiculum of the cornu ammonis. The neurons of the cerebral cortex were universally altered. The neurons of the second and third layers predominantly showed "water changes." † The neurons of other cortical layers showed "severe cell changes." † The astrocytic nuclei were enlarged and more vesicular than normal, and cytoplasmic processes tended to stain. Here and there a microglia nucleus was larger, and more vesicular, and cytoplasm showed staining. Oligodendroglia nuclei were condensed, and deeper-staining, and had a clear space about them. The degree of reactive changes of astrocytes in the first layer was such that mitotic figures were not uncommon. The endothelial nuclei of capillaries especially were large, numerous, rounded, and vesicular, and their cytoplasm stained more extensively than usual. This change in endothelium was present throughout the cerebral and cerebellar cortex, varied in intensity, was less marked in the brain stem, and was not clearly evident in the white matter. Acute swelling of oligodendrocytes was universal in the white matter.

Glial stars ‡ were numerous in the cortex and white matter of the cerebrum and were present in the brain stem. Two of these were in response to petechial hemorrhage. Certain ones had a green-staining sphere (Nissl's) in their midst, suggesting that the capillary lumen was occluded. Precipitated material in the Virchow-Robin spaces of the larger intracerebral vessels, in the gray and the white matter, was very noticeable. Often, a few mononuclear cells were present in this precipitated material. Some precipitated material was present in the subarachnoid space.

The cerebellum showed "homogeneous cell changes" of the Purkinje cells.‡ This change varied from folia to folia, with one-half the Purkinje cells so involved in certain folia. The "shrubbery" formation in the molecular layer was very conspicuous and seemed in excess of the number of neurons showing "homogeneous cell changes." The endothelial hypertrophy was very marked in the molecular layer. The granular layer of some folia showed focal areas of necrosis. Acute swelling of oligodendrocytes was present in the white matter. There was no activity of the connective tissue of the meninges of the cerebrum, cerebellum, and brain stem.

Here and there, overlying the sulci and at the cistern sites, there were a few mononuclear cells in the subarachnoid space. There were two petechial hemorrhages in the vicinity of the supraoptic nucleus and multiple older petechial hemorrhages in the third nerve nuclei. Polymorphonuclear cells and compound granular corpuscles had responded to this hemorrhage. This lesion had destroyed more tissue on one side of the midline than on the other.

Within the loosened meshes of the marginal glial layer, colonies of round cells, with a centrally placed round nucleus and a purple-staining cytoplasm with considerable white space therein, were observed. These colonies were observed at the surface of the sulci mostly. They were observed in a frontal section, the gyrus cinguli, and the cerebellum.

The lungs showed edema, congestion, and areas of bronchopneumonia. There was cloudy swelling of the liver. The kidney glomeruli were congested. The nuclei of the proximal tubules were pyknotic. The nuclei of the distal tubules were often greatly enlarged and showed inclusion bodies. The cytoplasm of collecting tubules was largely white space.

An Aerobacter aerogenes, Achromobacter, was cultured from a postmortem specimen from the brain stem and temporal lobe. No blood culture was made, either ante or post mortem.

† References 3 and 4.

‡ References 3 and 4.

The neuropathological findings in this case are more similar than dissimilar to those findings described in the literature under the classification of acute lead encephalitis or encephalopathy.§ The supposition that the changes in the brain have a relationship to the effect of blood lead levels on antibodies in the circulating blood was studied from the perspective of biochemistry.

Biochemical Considerations.—As is known, some metals have the propensity to precipitate proteins, and this precipitation apparently is selective in nature.[7] The gamma globulins are first affected; then other globulins, in a definite order. Thus, it is postulated that if the lead can precipitate gamma globulins, this action can also affect the antibody systems, since these are gamma globulins. To apply this postulate, the following procedures were carried out.

Aliquots of 1 cc. of serum from Type B blood were mixed with 0.01 cc. of varying dilutions of a lead nitrate solution so that the concentration of lead in each aliquot was 0.03, 0.12, 0.30, and 0.90 mg. per 100 cc., with one untreated aliquot serving as a control. These mixtures were incubated at 37 C. for one-half hour. Then to each aliquot was added 0.2 cc. of red cells from Type A blood.

Since the alpha isoagglutinins of Type B blood are gamma globulins and should be inactivated by lead, the amount of precipitation of red cells should likewise be affected. This was found to be true to a certain degree.

The aliquot of treated serum which contained 0.12 mg. per 100 cc. of lead was found to give a definitely smaller amount of precipitation than did either the control or the aliquot treated with 0.3 mg. per 100 cc. of lead.

The disturbing factor was that the aliquots treated with 0.30 and 0.90 mg. per 100 cc. of lead produced more of a precipitate than did any of the rest, including the control.

On examination of this simple test, it was postulated that the highest concentrations of lead were sufficient to cause reaction with other proteins as well as with the gamma globulins.

To determine whether all the isoagglutinins (gamma globulins) were affected, the supernatant fluid from the test tubes was titrated for the presence of remaining isoagglutinins. There were titratable isoagglutinins still present in Tubes 1 and 2, but none were present in Tubes 3, 4, and 5. This finding is presumptive evidence that the isoagglutinins were inactivated by the lead.

As can be seen from the above description, the apparent greatest effect on the gamma globulins alone was at a concentration of 0.12 mg. per 100 cc. This is the accepted dangerously toxic level of lead in the blood.[8] This being so, it can further be postulated that the greatest effect of this lead concentration in the human being would be on the gamma globulins and the antibody system; therefore, it can further be assumed that the line of defense of the body against an infection occurring and running wild would be broken or destroyed.

It would seem, then, that the antibodies can be inactivated if they already exist, and most probably after they are formed, if they are formed.‖

COMMENT

We might wish we had blood cultures in this instance. Blood cultures in case reports in the literature are noticeably absent. This omission is understandable, since attention has been focused on the direct effect of lead itself.

Blackman states that fever and marked leucocytosis occur. These signs could be construed as an expression of blood stream infection.[5] Ford states that acute infections and various conditions such as may lead to acidosis seem to play a role in precipitating the development of symptoms.[11]

Comment has been limited to bacterial invasion and growth. It follows that virus invasion and growth in the circulating blood may be similarly affected.

§ References 5 and 6.

‖ References 9 and 10.

Acute deaths in lead intoxication are commoner in childhood than in adulthood. The inference would be that the factor of inactivation of antibodies in the circulating blood is not as prominent in adulthood as in childhood. This possible difference is something to be studied.

Blackman observed the presence of an exudate which he considered had coagulated in the tissue before death.[5] He comments that the mechanism of this coagulated exudate remains obscure. This exudate which Blackman has observed, and which is present in this case, may be the expression of the process involved in the inactivation of antibodies.

Should this inactivation of antibodies, particularly in childhood, come to be an established fact, then treatment considerations will need revision. There will still be the need to reduce the lead level. There will be the need to replace antibodies by giving either gamma globulin or immune serums. The need for a bactericidal rather than merely a bacteriostatic drug is obvious.

CONCLUSIONS

Antibodies are inactivated by lead. The level of lead in the circulating blood which affects the antibodies is in the critical range of about 0.12 mg. per 100 cc.

This inactivation of antibodies diminishes the defenses of the circulating blood to the invasion and growth of injurious agents, such as bacteria.

Through this inactivation, the pathological changes in the central nervous system may be the result of the toxic products of the less inhibited growth of infectious agents. In those instances in which the lead blood level exceeds the critical range, the elapsed time may not have been sufficient for the manifestations of the direct toxic effect of the lead.

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STUDIES OF 17-HYDROXYCORTICOSTEROIDS

VIII. Adrenocortical Function in Patients with Convulsive Disorder

PATRICK F. BRAY, M.D.
ROBERT S. ELY, M.D.
AND
VINCENT C. KELLEY, M.D., Ph.D.
SALT LAKE CITY

SEVERAL different lines of investigation have supported the concept that function of the pituitary-adrenal system is one factor operating in the production of altered states of consciousness. Mental disorders, seen in patients with Addison's disease,* have been reported to respond to treatment with desoxycorticosterone acetate (DCA), cortisone, or corticotropin (ACTH).[3] On the other hand, a variety of mental disorders has been described in patients receiving corticotropin or cortisone.† In addition, numerous clinical reports indicate that patients may develop convulsions during corticotropin or cortisone treatment of apparently unrelated conditions.‡

The occurrence of convulsions during hormonal therapy is in keeping with the experimental observation that cortisone and other biologically active 17-hydroxycorticosteroids increase brain excitability in animals, as measured by the depression of the electroshock threshold.[12] Additional evidence of the effect of these hormones on the electrical activity of the brain has been provided by electroencephalography. EEG abnormalities long have been described in some patients with Addison's disease,[13] and these abnormalities have subsided on hormonal therapy.[4] There have been several reports of EEG changes in patients receiving corticotropin or cortisone for other conditions, but the direction and nature of the changes have not been consistent.§

Some of the therapeutically beneficial anticonvulsant drugs appear to have as one of their actions an influence on adrenocortical function. Diphenylhydantoin (Dilantin), when chronically administered to rats, causes a significant increase in the weight of the adrenal glands,‖ providing evidence [16] that this drug stimulates

From the Lockhart Memorial Laboratory, Department of Pediatrics, University of Utah School of Medicine.

H. Beth Dowding, Margaret G. Anderson, Doris F. Tippit, Helen Birch, and Mary C. O'Brien gave technical assistance in this study.

* References 1 and 2.

† References 4 through 8.

‡ References 9 through 11.

§ References 4, 5, 14, and 15.

‖ References 16 and 17.

the pituitary-adrenal system. In intact animals, single doses of diphenylhydantoin have no effect on brain excitability.[17] In contrast, it has been shown recently by Woodbury [19] that in adrenalectomized animals a single dose of diphenylhydantoin produces a definite and sustained decrease in brain excitability. These data would suggest that the action of diphenylhydantoin is modified by the functional state of the adrenal gland.

In recent years new techniques have been developed which permit a more direct evaluation of adrenocortical function. The method developed by Nelson and Samuels [20] measures the circulating plasma 17-hydroxycorticosteroids, the predominant steroids produced by the adrenal cortex. Included in this group of steroids are cortisone and hydrocortisone, the latter being the principal adrenocortical hormone in man.

In an attempt to determine whether an altered state of adrenocortical function exists in patients with convulsive disorder, the present investigation was undertaken. This preliminary report is concerned with data obtained in these studies, which include measurements of plasma 17-hydroxycorticosteroid levels and their response to the administration of corticotropin.

MATERIALS AND METHODS

The subjects used in this study include a well (control) group of 40 children and a group of 47 children and young adults with convulsive disorder. The latter patients were divided into the following categories:

Group I: Thirteen subjects who had convulsive disorder, untreated

Group II: (*a*) Nineteen patients who had received chronic diphenylhydantoin therapy (more than two months) and (*b*) 15 patients who had received chronic anticonvulsant therapy other than diphenylhydantoin.

Because of the relatively small number of cases, no division of patients according to clinical or electroencephalographic seizure types has been made.

Plasma 17-hydroxycorticosteroid concentrations were determined by the method of Nelson and Samuels,[20] eosinophiles by the method of Randolph,[21] and glucose by the method of Nelson.[22] These determinations were performed before and at intervals following the intramuscular administration of 25 international units (I. U.) of corticotropin.¶ The 17-hydroxycorticosteroid responses were determined two hours after the administration of corticotropin, as has been described as a standard corticotropin-steroid response test [23]; the eosinophile and glucose responses to corticotropin were determined at one, two, and four hours.

RESULTS

To evaluate adrenocortical function in the groups of patients with convulsive disorder, reference is made to the well (control) group, whose adrenocortical function is assumed to be normal. Data concerning this latter group are presented elsewhere.# The fasting concentrations of total circulating eosinophiles, glucose, and 17-hydroxycorticosteroids in the different groups of subjects are shown in Table 1. None of the groups differed significantly from normal with regard to any of these values.

In Table 2 are shown the responses of total circulating eosinophiles and of glucose following the administration of corticotropin. An adequate eosinopenia occurred in both the nontreated and the treated group of convulsive disorder patients.

¶ ACTHAR supplied through the courtesy of the Armour Laboratories, Chicago.

References 23 and 24.

On the other hand, the glucose response to corticotropin differs between these groups. Whereas this response in the nontreated epileptic group was similar to that in the control group, the response in the treated group was significantly less than normal ($P < 0.01$). However, because of the large standard error of the mean (S.E.) in the nontreated group, the difference in glucose response between this group and the treated group was not significant.

TABLE 1.—*Initial Eosinophile, Glucose, and 17-Hydroxycorticosteroid Values* in Patients with Convulsive Disorder*

Group	Eosinophiles, per Cu. Mm. Blood			Glucose, Mg. per 100 Cc.			Plasma 17-Hydroxycorticosteroids, γ/100 Cc.		
	No.	Mean	S. E. M.	No.	Mean	S. E. M.	No.	Mean	S. E. M.
Normal	40	187	15.6	40	76	2.6	40	12.0	1.29
Convulsive disorder, nontreated	13	212	39.4	13	84	3.9	8	13.7	1.89
Convulsive disorder, treated	33	187	21.3	33	81	2.5	34	11.5	1.22
(*a*) Diphenylhydantoin	19	168	24.2	19	77	2.1	19	11.2	1.42
(*b*) Other medication	14	213	34.4	14	86	4.1	15	12.0	2.15

* $P > 0.05$ when the value of any group is compared with that of the normal group in each column. Thus, none of the groups differ significantly from normal with regard to any of the variables studied.

TABLE 2.—*Eosinophile and Glucose Responses to Corticotropin in Patients with Convulsive Disorder*

Group	Eosinophile Response, Maximum % Decrease				Glucose Response, Maximum Increase, Mg. per 100 Cc.			
	No.	Mean %, Depletion	S. E. M.	*P*	No.	Mean, Increase	S. E. M.	*P*
Normal	40	52	± 6.6	.....	40	12	2.4	.....
Convulsive disorder, nontreated	13	64	±14.7	>0.05	13	12	7.2	>0.05
Convulsive disorder, treated	33	52	± 9.4	>0.05	33	5	2.5	0.05

TABLE 3.—*17-Hydroxycorticosteroid Response to Corticotropin in Patients with Convulsive Disorder*

Group	No.	Plasma 17-Hydroxycorticosteroids, γ/100 Cc.				
		0 Hr. Mean	2 Hr. Mean	Mean Increase	S. E. M.	*P*
Well (control)	40	12.0	29.8	17.8	1.76	.....
Convulsive disorder, nontreated	10	13.7	25.9	12.2	3.70	>0.05
Convulsive disorder, treated	34	11.5	20.6	9.1	2.20	<0.01
(*a*) Diphenylhydantoin	19	11.2	17.8	6.6	3.08	<0.01
(*b*) Other medication	15	12.0	24.2	12.2	3.08	>0.05

Responses of plasma 17-hydroxycorticosteroid concentrations to corticotropin are shown in Table 3. As mentioned concerning the data in Table 1, the initial steroid values are essentially the same in all groups. However, the mean values two hours after corticotropin administration differ considerably among these groups. This is demonstrated more clearly by the data in the column showing the magnitude of elevation in response to corticotropin. The mean steroid elevation of 12.2 γ per 100 cc. in the nontreated convulsive disorder group was less than, but not significantly different from, that of 17.8 γ per 100 cc. shown by the well (control)

group. In the treated convulsive disorder group, however, the mean steroid elevation was only 9.1 γ per 100 cc. This response is significantly less than that of the control group, $P < 0.01$. When the treated group is divided into the chronically diphenylhydantoin-treated epileptics and those chronically treated with medication other than diphenylhydantoin, an interesting difference between the two groups is seen. Although the initial mean plasma 17-hydroxycorticosteroid level is adequate in the diphenylhydantoin-treated group, the mean steroid elevation following corticotropin is only 6.6 γ per 100 cc., significantly less than that in the control group. On the other hand, the steroid response in the other treated group is 12.2 γ per 100 cc., not significantly different from that in the control group. In spite of the apparent large difference between the steroid responses shown by these two treated groups, statistically this difference is not significant.

COMMENT

Evaluation of the role of the pituitary-adrenocortical system in influencing seizures has been difficult. McQuarrie, Anderson, and Ziegler [25] focused attention on a possible endocrine relationship when they used DCA therapeutically with good results in two patients with epilepsy. Similar results were reported by Aird and Gordan,[26] who found a beneficial anticonvulsant effect in 10 epileptics when sublingual DCA was used as an adjuvant to standard drug therapy. In contrast to these beneficial effects of DCA, detrimental effects leading to seizures may be produced by corticotropin and cortisone.* These clinical observations of antagonistic effects are in accord with the results of animal investigations, which demonstrate a similar antagonistic action between DCA and corticotropin or cortisone on brain excitability.†

Such observations suggest that an altered state of adrenocortical function may be a factor in the genesis of convulsive disorder. However, results of investigations which have been made to evaluate this possibility, employing indirect criteria of adrenocortical function, have allowed only inconclusive interpretations.‡ In the present investigation, similar indirect criteria of adrenocortical function, eosinophile and glucose responses, were measured. In addition, however, a more direct index of adrenal function was obtained by studying the plasma concentrations of 17-hydroxycorticosteroids.

The plasma 17-hydroxycorticosteroid response to corticotropin has been presented [28] as a test which will assess directly adrenocortical secretory activity. This test can identify those patients in whom adrenocortical function is absent or considerably diminished, both by their low initial plasma steroid levels and by the failure of these levels to become elevated after corticotropin administration. Among other tests of adrenal function the most widely used are the eosinophile responses to epinephrine or corticotropin. The epinephrine-eosinophile response test no longer is considered a valid measure of adrenal function.§ The corticotropin-eosinophile

* References 9 through 11.

† References 12 and 27.

‡ References 28 through 31. Holler, J. W.; Burton, R. B.; Dury, A., and Keutman, E. H.: Effect of Epinephrine on the Serum Potassium Levels in Adrenal Insufficiency, unpublished data, cited by Dury, Holler, and Smith.[31]

§ References 32 and 33.

response test cannot be depended upon to detect altered states of adrenocortical function, other than that of frank insufficiency.[23] Since these inadequacies of the eosinophile response tests are less apparent with the corticotropin-17-hydroxycorticosteroid reponse test, the latter may be considered more reliable for evaluating adrenocortical function.

Neither of the indirect criteria of adrenocortical function employed in this study, the eosinophile or the glucose response test, gave any strong indication of abnormal adrenocortical function in patients with convulsive disorder. The total circulating eosinophile count and eosinopenic response to corticotropin in all epileptic groups were comparable to those in the normal group. Interpretation of the corticotropin-glucose response data, as obtained in these groups, was difficult. Generally, blood glucose response to corticotropin has been studied in terms of repeated corticotropin administration or of the influence of corticotropin on the glucose tolerance curve.‖ The response of blood glucose to a single injection of corticotropin has been studied only little and has not been evaluated completely.[38] It therefore is difficult to interpret the interesting observation that the hyperglycemic response to corticotropin in the group of treated convulsive disorder patients was less than that in the control group or that in the group of untreated epileptics.

On the other hand, the more direct criterion of adrenocortical function, the corticotropin-steroid response test, did yield data strongly suggesting that the functional state of the adrenal cortex, although not abnormal in the convulsive disorder patient, becomes altered under the influence of diphenylhydantoin therapy. The poor corticotropin-steroid response in the diphenylhydantoin-treated group, as opposed to the normal steroid response in untreated epileptic patients, suggests that chronic diphenylhydantoin therapy actually produces a degree of adrenocortical unresponsiveness in the subject with convulsive disorder.

The evidence that diphenylhydantoin causes an increase in adrenal weight [18] would appear to oppose such an interpretation, as would the fact that the decrease in brain excitability produced by a single injection of diphenylhydantoin in adrenalectomized animals [19] does not occur in intact animals similarly treated.[17] These findings suggest that diphenylhydantoin has a direct action on the central nervous system, decreasing brain excitability, and an indirect action through the adrenal gland, increasing brain excitability. Since 17-hydroxycorticosteroids are the predominating adrenal steroids in man and since these steroids increase brain excitability in animals,[12] the inference is drawn that this adrenal effect on brain excitability is mediated through the production of these 17-hydroxycorticosteroids. On the other hand, chronic diphenylhydantoin administration in intact animals effects a decrease in brain excitability.¶ Also, several days of diphenylhydantoin therapy are required before beneficial effects are observed in control of the convulsive patient. Thus, diphenylhydantoin may stimulate the adrenal cortex initially but produce in time a state of relative adrenal unresponsiveness. The poor 17-hydroxycorticosteroid response to corticotropin reported here in the diphenylhydantoin-treated group of patients indicates that such adrenal unresponsiveness does occur.

‖ References 34 through 37.

¶ References 17 and 19.

Theoretically, this adrenal unresponsiveness would bring about a decrease in brain excitability. This may be one important factor in the mechanism of action of diphenylhydantoin. No attempt was made to evaluate this possibility in the present study, since the size of the diphenylhydantoin-treated group was too small and the clinical criteria too complex to permit any meaningful comparison of steroid response with clinical response.

SUMMARY

Adrenocortical function was studied in subjects with convulsive disorder. Response tests used were the eosinophile response to corticotropin, the glucose response to corticotropin, and the plasma 17-hydroxycorticosteroid response to corticotropin.

Although the eosinophile response to corticotropin was adequate in all groups, the steroid response to corticotropin in those patients receiving diphenylhydantoin was reduced very significantly as compared with the control group.

This observation in the diphenylhydantoin-treated group is discussed. The suggestion is made that diphenylhydantoin therapy produces a relative adrenocortical unresponsiveness which may be a factor in the action of diphenylhydantoin on brain excitability.

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CONTROL OF TWO SIMULTANEOUS VOLUNTARY MOTOR ACTS IN NORMALS AND IN PARKINSONISM

ROBERT S. SCHWAB, M.D.
MORRIS E. CHAFETZ, M.D.
AND
SYLVIA WALKER, R.N.
BOSTON

BECAUSE of the multiple and varied aspects of Parkinsonism, the therapeutic approach has been exceedingly difficult. Most efforts have been directed toward symptomatic control of rigidity and tremor. The atropine-like drugs have been relatively successful in alleviating rigidity in patients able to tolerate adequate amounts.[1] Parsidol (10-[2-diethylamino-1-propyl] phenothiazine hydrochloride) [2] has been reasonably effective in some patients in reducing tremor, and by various drug combinations and the individualizing of dosages [3] many Parkinsonian patients continue to lead active, useful lives.

A common complaint of the Parkinsonian patient is related, however, to fatigue and slowness in performing the chores of ordinary life. This is attributed to the interference caused by the muscle rigidity and tremor. In 50 patients with Parkinsonism, visual-motor reaction time tests have been routinely performed, and the values are close to normal in mild and moderately severe cases. In the course of observing a large number of Parkinsonian patients in the private practice and clinic setting, it became apparent that another motor impairment beside tremor and rigidity was present. This symptom complex we describe as the inability to maintain at the same time two voluntary motor activities.

This impairment is not to be confused with the so-called associated motor movements, such as swinging the arms when walking, turning both the eyes and head when looking to the side, etc. These latter examples are reflex motor components of a single voluntary pattern which renders movement more efficient and easier to perform. The loss of associated movements is one of the earliest deficits noted in Parkinsonism and is sufficiently well described and documented in the literature

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From the Departments of Neurology and Psychiatry, Harvard Medical School, and the Neurological and Psychiatric Services at the Massachusetts General Hospital.

Clinical Assistant Professor in Neurology, Harvard Medical School, and Neurologist, Massachusetts General Hospital (Dr. Schwab). Research Fellow in Psychiatry, Harvard Medical School, and Clinical Fellow in Psychiatry, Massachusetts General Hospital (Dr. Chafetz).

to exclude repetition here. Impairment of the ability to maintain two separate motor activities at the same time is a conspicuous feature of nearly all patients suffering from Parkinson's disease, and it is with this entity that this paper is to deal.

TECHNIQUE OF TEST

When we became aware of this impairment in the Parkinsonian patient, we felt it necessary to establish a quantitative test of this function. Since we routinely obtain a voluntary bulb ergogram of the right and left grip in our examination of all patients (Fig. 1), it was simple to obtain a control ergogram of the nondominant hand while the dominant hand performed another motor act. The two ergographic curves were then compared, and the amount of combined motor activity lost was measured quantitatively. The task of the dominant hand has been arbitrarily set at tracing the outline of a triangle and drawing three perpendicular lines

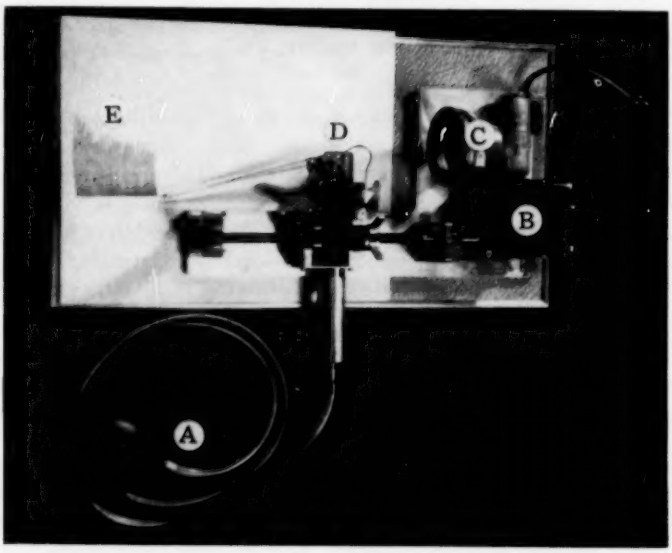

Fig. 1.—Portable hand bulb ergograph. *A*, rubber bulb held in either hand; *B*, synchronous motor; *C*, bell signal once a second activated by cam with each revolution of the shaft; *D*, carriage on worm shaft with air cylinder, spring, inkwell, and write-out pen. Note spring release on right of carriage which permits return of carriage to zero position on left end of worm shaft. *E*, ergogram.

This unit is made at the Harvard Medical School Machine Shop (Mr. Christiansen).

in addition, a total of six drawn lines. While this was being done, the other hand squeezed the ergographic bulb, with the whole procedure timed by a stop watch.

Patients were obtained from both private practice and clinic, as noted above. A total of 150 Parkinsonian patients have been tested over a two-year period. Control studies using this "combined test" have been done in all decades from 10 to 80 years. A total of 50 control subjects were studied, and they were free from any neurological or other severe disease as far as we could determine. The controls consisted of laboratory technicians, staff and visiting physicians, and other hospital personnel. The tests were administered by a trained nurse (S. W.) and were then scored in relation to the single ergographic performance as to amplitude maintenance, gap formation, and speed of performance.

To eliminate the possibility that the control subjects were not drawing the lines and squeezing the ergographic bulb simultaneously, a triangle with metal points was constructed and the

recordings in some cases were made on the EEG machine (Fig. 2). In the control group the combined ergographic response is maintained as relates both to amplitude and to absence of gap formation (Fig. 3). In Figure 4 one notes a control whose test was performed rather slowly (23 seconds), but whose amplitude and simultaneous movements were controlled and maintained.

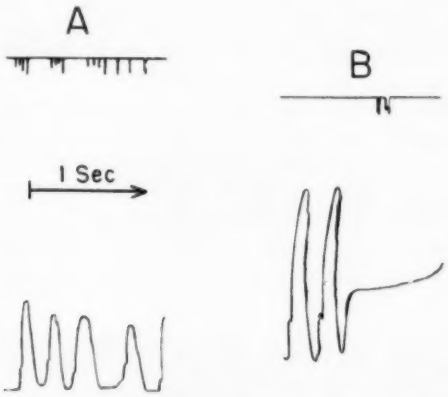

Fig. 2.—*A*, portion of tracing of combined test on normal control, showing simultaneous drawing and squeezing. *B*, tracing of a patient with Parkinson's disease doing combined test, showing consecutive squeezing and drawing.

In *A*, 15 of 18 contact points in triangle were touched in the 1.4 seconds of the sample (task completed in 1.8 seconds), whereas in *B*, in the same time only 2 of the contact points were touched by the patient.

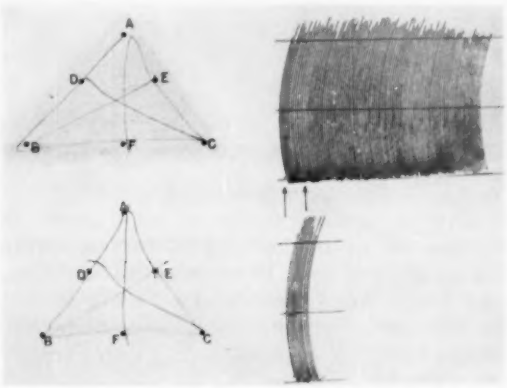

Fig. 3 (normal subject).—Lower half illustrates combined test. Triangle was drawn with dominant hand, while ergographic bulb was squeezed with nondominant hand. Time of test 5 seconds.

Subjects drew from points *A* to *B*, *B* to *C*, *C* to *A*, *A* to *F*, *B* to *E*, and *C* to *D*.

Arrows indicate equivalent period of single ergogram (with nondominant hand) in upper portion.

Triangle in upper left drawn with dominant hand in 3 seconds without use of ergogram.

Clinically, the impairment we wish to describe may be clearly stated through the use of a number of examples. A normal subject maintains an interesting conversation when walking down the street with another person, negotiating obstruc-

tions, and avoiding hazards in traffic. Another example may be the wielding of a razor with the right hand, while the left hand skilfully tightens and manipulates the skin area being shaved. Getting out of a taxicab involves a complicated postural motor pattern in going from the seat to the erect position and in opening the door with the left hand while reaching into a pocket to procure change with the right hand. These are familiar examples of this ability, and they are essential properties of the motor acts of intelligent man necessary in maintaining the efficiency of everyday life.

In the Parkinsonian patient this ability is impaired. For example, a patient with Parkinson's disease seated in a hotel lobby notes an acquaintance entering the door. He starts to rise from the chair, which is motor activity No. 1, a complicated postural action involving balancing of the body as it reaches the erect position. After this motor activity has been started and is perhaps 50% completed, the normal pattern would include the extension of the right hand in greeting the acquaintance, a second motor activity not related to the first. The person without Parkinsonism

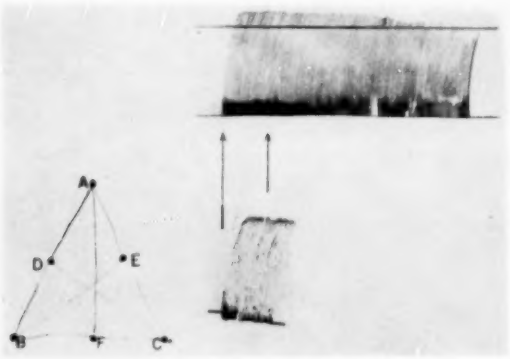

Fig. 4 (normal subject).—Lower half illustrates combined test. Test time 23 seconds. Single ergogram is in upper portion.

Note absence of gap formation and amplitude maintenance.

will execute these two motor patterns without difficulty so that they blend into a smooth complex of social behavior. However, when the Parkinsonian patient starts the second motor act, he finds that the first one has ceased. This results in his falling back into his chair in an embarrassing and unceremonious manner. If he again attempts to get out of the chair, the second motor activity of the greeting ceases and the right arm falls awkwardly. In this struggle to perform successfully these common motor acts the Parkinsonian patient is left in a state of agitated frustration and anger, which leads to an increase in rigidity and tremor. This state results in a simple social act, causing a stressful situation. Other difficulties occur daily in the combined activities of feeding, dressing, toilet habits, etc.

REPORT OF CASES

This aspect may be illustrated by two case histories.

Case 1.—S. E., a 58-year-old business executive, had developed subjective stiffness and awkwardness in his left arm and leg four years previously. There has never been any tremor

or any involvement of the right side. Loss of associated movements on the left side was noted during the beginning of his illness. A slight amount of cogwheel rigidity has always been present on the left but not on the right. He has always been unusually sensitive to the belladonna drugs, and the synthetic compounds, such as trihexyphenidyl (Artane) hydrochloride, Parsidol, and caramiphen (Panparnit) hydrochloride, have never been tolerated except in tiny doses.

At first it was difficult to see why, in view of the small amount of rigidity and the absence of tremor, he was so unhappy about his illness. When the combined test was initiated, however, it was apparent that this deficit was the severest of his symptoms. After explaining the purpose of the test to the patient, he recounted with great interest numerous examples of the frustrating annoyance of this impairment; e. g., when walking across the hotel lobby in front of the usual number of strangers to pay his bill, he reached into his inside pocket with his left hand to get his wallet. At once he stopped walking, standing immobile before the strangers. Becoming aware of this, he then resumed walking but his left hand remained in his inside pocket, suggesting perhaps a planned holdup. All of this produced anxiety, tension, and frustration in the patient and ended in his precipitous flight to his room to recover.

In the combined test the interruptions of the ergogram produced by the left hand were six in number and showed that each time he drew a line with his right hand, the left hand

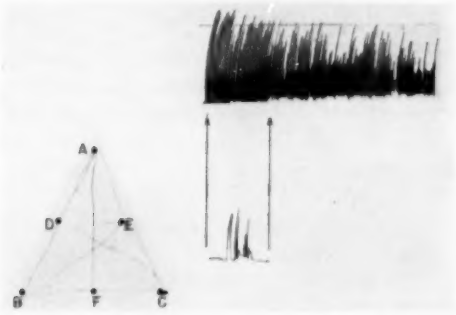

Fig. 5.—Response of subject in Case 1. Combined test 17 seconds. Compare deterioration of response in combined ergograph with equivalent area of single ergogram in upper portion.

stopped moving (Fig. 5). The total time needed to perform the test was 20 seconds, which is three times that of a normal control for the same age group. As far as therapy is concerned, it has not been successful in improving this deficit in the patient.

Case 2.—M. T., a 50-year-old surgeon with bilateral rigidity and minimal tremor of two years' duration, had great difficulty with the combined test, although his separate ergographic performance was nearly normal. When he was adequately adjusted on trihexyphenidyl hydrochloride and phenindamine (Thephorin) tartrate, the rigidity was reduced and the combined test significantly improved. Subjectively, with this development, the patient noted that he dressed more quickly and was able to participate in some surgical procedures, and there was greater ease in getting about and doing his chores.

The "combined test" we have described measured this defect. In some patients the single ergographic test was performed with relative ease and satisfaction. However, when the second motor act was instituted, the ergographic response would yield gap formation (Fig. 5) and an erratic amplitude. The test was generally more slowly performed, although this factor was not always the most striking feature. In many cases the tests were produced only by consecutive movements; i. e., the patient would draw one line, then squeeze, then draw, and this resulted

in a pattern with six gaps and was most striking. The test sometimes caused the subject to show frustration associated with increased tremor, flushing, and perspiration. In some patients, minimum or no tremor and very little rigidity were present, and yet they produced combined tests which were very poor.

In Figure 6 is illustrated the combined test of one patient without his Parkinsonian medication. The typical gap formation and falling off of amplitude are clearly

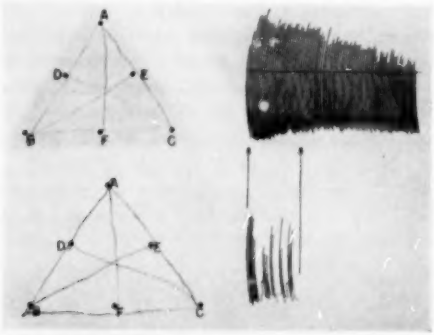

Fig. 6.—Parkinsonian patient without medication. Combined test 19 seconds, with gap formation and amplitude decrements. Note single ergographic response on upper right side, and single triangle on left drawn in 11 seconds.

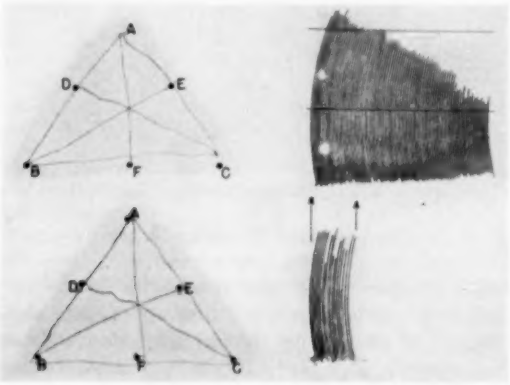

Fig. 7.—Same patient as in Figure 6, two days after being placed on medication. Combined test in 15 seconds. Note amplitude maintained and absence of significant gap formation. Test could be described as within normal limits. Single triangle drawn in 10 seconds.

to be noted. In Figure 7 is shown the ergographic response of the same patient following the resumption of his medication.

In some cases the successful effect of drugs on the tremor and rigidity fails to improve the combined-test difficulty. In other patients the combined tests show a sufficient degree of improvement that they are considered normal (Fig. 7). As a group, the Parkinsonian patients perform the combined test with difficulty associated with slowness, disturbed amplitude, and gap formation.

COMMENT

The inability of the Parkinsonian patient to maintain concurrent movements is of interest from both the physiological and the emotional point of view. The normal person initiates a rather complicated learned pattern and maintains this under efficient operational control; he then begins a second motor act, involving a completely different set of muscles, which is, therefore, continued and maintained efficiently without any interference whatsoever with the first act. At the same time he may be thinking of other things. The division into controlling elements of consciousness that allows two, and even three, separate patterns to be controlled at the same time is, of course, not physiologically understood. Denny-Brown [4] has suggested that the basal ganglia and subthalamic nuclei are the essential sites for motor integration of stereotyped behavior, although he offers no information as to how this is accomplished. If this holds true, then a lesion in the basal ganglia [5] may produce the impairment in Parkinsonian patients which we have described.

This impairment in ability to perform motor activities concurrently raises a practical point. If the Parkinsonian patient cannot perform acts concurrently, he must then execute them in consecutive order. Therefore, if one has 21 separate motor movements to perform in getting dressed, for example, and one is forced to carry all these out one after another, then the completed act of dressing will require considerably more time than the normal concurrent approach. This will, then, most likely be responsible for a good deal of the slowness noted with Parkinsonian patients. Actual measurements in our laboratory bear this out. Measurement of an individual visual-motor act by patients with Parkinsonism show a surprisingly normal speed of muscular performance (motor reaction time is often normal or only 10 to 15% prolonged). Many Parkinsonian patients can do individual motor acts, such as drawing circles, in only slightly more time than is taken by a normal control. However, with severe rigidity and in advanced cases both the increased reaction time and the increased loss of ability to perform concurrent motor acts are present.

In patients who have this deficit to a marked degree, their usual method of dealing with it is to try harder and harder to perform as a normal, each time resulting in conspicuous failure leading to increased frustration. Other patients who have a high degree of adaptability learn to accomplish tasks by approaching them in a consecutive manner. There is elimination of useful and normal concurrent motor activity pattern, which leads to excessively ritualistic and overdeliberate reaction patterns suggestive of obsessive-compulsive personalities. The emotional responses to this impairment will be dealt with in a later paper.

An interesting finding was noted in our study of normal controls. It was evident that a tendency to impaired functioning in this test begins to show up in the seventh and eighth decades in patients who do not have Parkinson's disease. However, the comparison between these subjects and those with Parkinson's disease in the same age group shows differences that are four to five times greater. Apparently, there is a slight but definite progressive loss of this function in the normal aging process of human beings. We have no data as yet of the deficits of this test in mild cases of pyramidal tract disorder or in other neurological conditions.

It has been suggested that the word "synkinesia" describes the normal function discussed in this communication, and "asynkinesia," the deficit common to Parkinson's disease.

SUMMARY

1. Material concerning an impairment found in Parkinsonism is presented.

2. An objective test to measure deficits related to this impairment is discussed.

3. Normal control results are correlated with those seen in Parkinsonian patients.

4. Physiological and emotional difficulties related to the difficulty of maintaining two separate motor acts in Parkinsonism are considered.

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EFFECT OF CORTISONE ACETATE ADMINISTERED INTRACISTERNALLY IN CATS

MONI SAMUELOFF, M.D.
AND
SHAUL FELDMAN, M.D.
JERUSALEM

THE PRESENT study was undertaken in order to examine the effect on cats of intracisternally administered cortisone acetate. The investigation was considered to be both of theoretical and of practical interest in view of the effect of cortisone on normal function, as well as its influence in certain pathological conditions of the nervous system. This investigation includes acute and chronic experiments and pathological examinations.

METHODS

(*a*) *Acute Experiments.*—This group consisted of eight cats. The experiments were conducted with pentobarbital (Nembutal) anesthesia, 20 mg. of the anesthetic being administered per kilogram of body weight, and the duration of the experiments was from two to three hours. Blood pressure, from the femoral artery, respiration, and electroencephalographic tracings, taken from two symmetrical parietal electrodes, were recorded throughout the experiments. A number of experiments were performed on the same animal at intervals of one hour, at which times the blood pressure and respiration readings were normal. Different quantities of cortisone acetate (Cortone acetate), viz., 1, 1.5, 2, 2.5, 3, 10, and 12 mg. per kilogram of body weight, were introduced into the cisterna magna. Before the injection a quantity of cerebrospinal fluid, corresponding to the volume of cortisone suspension introduced, was withdrawn.

Benzyl alcohol, which is contained in the cortisone acetate suspension used in our experiments, was introduced intracisternally in five cats, in a concentration of 0.9% and in quantities equal to those previously administered with the higher doses of cortisone acetate. In two animals, 0.5 and 1 cc., respectively, of isotonic sodium chloride sodium, which is the suspending agent of the hormone, was introduced.

(*b*) *Chronic Experiments.*—A total of 20 cats were used in these experiments. Cisternal taps were performed with the animals under ether anesthesia. Immediately prior to the injection 0.5 cc. of C. S. F. was removed. Of these cats, 13 received a single injection of cortisone in quantities ranging from 1 to 8 mg. per kilogram of body weight. The puncture was repeated in various animals of this group after 24, 48, and 72 hours, as well as on following days up to the ninth day after the single cortisone administration. The C. S. F. withdrawn was examined for cells, and the Pandy test was performed. In five animals total nitrogen and N. P. N. in the C. S. F. were determined by the micro-Kjeldahl method, and protein nitrogen was calculated.

Seven cats received repeated intracisternal injections of cortisone, at intervals of two or more days, in doses of 1 to 2 mg. per kilogram of body weight. Preceding each injection of cortisone, 0.5 cc. of C. S. F. was removed, and cell counts and Pandy tests were made.

In eight animals a single injection of 0.3 to 1 cc. of isotonic saline was made intracisternally.

From the Department of Neurology, Rothschild-Hadassah-University Hospital, and the Department of Physiology, Hebrew University, Hadassah Medical School.

(*c*) *Pathological Examinations.*—The brains and spinal cords of three animals which had received 7, 10, and 11 intracisternal injections of cortisone, respectively, during the course of a month, were examined.

RESULTS

(*a*) *Acute Experiments.*—The administration of 1 or 1.5 mg. of cortisone per kilogram of body weight caused no appreciable changes in the blood pressure, respiration (Fig. 1), or electroencephalogram. In cats receiving 2, 2.5, or 3 mg. of cortisone per kilogram of body weight, a slight drop of blood pressure, a decrease in tidal air, and a slowing of respiration were recorded. These changes lasted from 15 to 20 seconds, and the blood pressure and respiration then returned to normal. No electroencephalographic changes were observed.

On the other hand, injection into the cisterna magna of higher doses of cortisone caused a very marked and immediate drop in blood pressure, as well as apnea, which

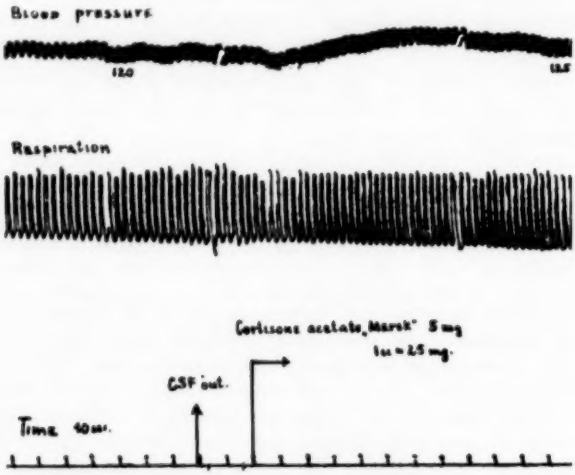

Fig. 1.—Effect on blood pressure and respiration of 1.5 mg. of cortisone per kilogram of body weight introduced intracisternally.

lasted from 20 seconds to 4 minutes (Fig 2*A*). At the same time, the EEG record showed a slowing of rhythm and eventually became flat, to return to normal when the blood pressure and respiration became normal. The injection of a solution of 0.9% benzyl alcohol in quantities corresponding to those contained in the higher doses of cortisone acetate caused a drop in blood pressure and apnea similar to that seen after the injection of the hormone suspension (Fig. 2 *B*). No changes were observed during the intracisternal injection of isotonic saline.

(*b*) *Chronic Experiments.*—1. Effect of a Single Injection of Cortisone: Prior to the administration of cortisone the C. S. F. contained no cells and the Pandy test was negative. Twenty-four hours after the intracisternal injection of cortisone the C. S. F. showed a considerable pleocytosis. In some animals, the white cell count reached more than 1,000 cells per cubic millimeter, and the Pandy test became positive in all the samples. After 48 hours, the pleocytosis decreased considerably, with a mean count of 64 per cubic millimeter, while after 72 hours it

went down to 23 white cells per cubic millimeter. From the fourth day onward, only a few cells were found in the cisternal fluid (Fig. 3). The protein estimation showed changes which paralleled those of the white cell count, a rise in protein after 24 hours and then a gradual decrease (Fig. 4). No correlation was found between the quantities of cortisone administered and the degree of pleocytosis. The injection

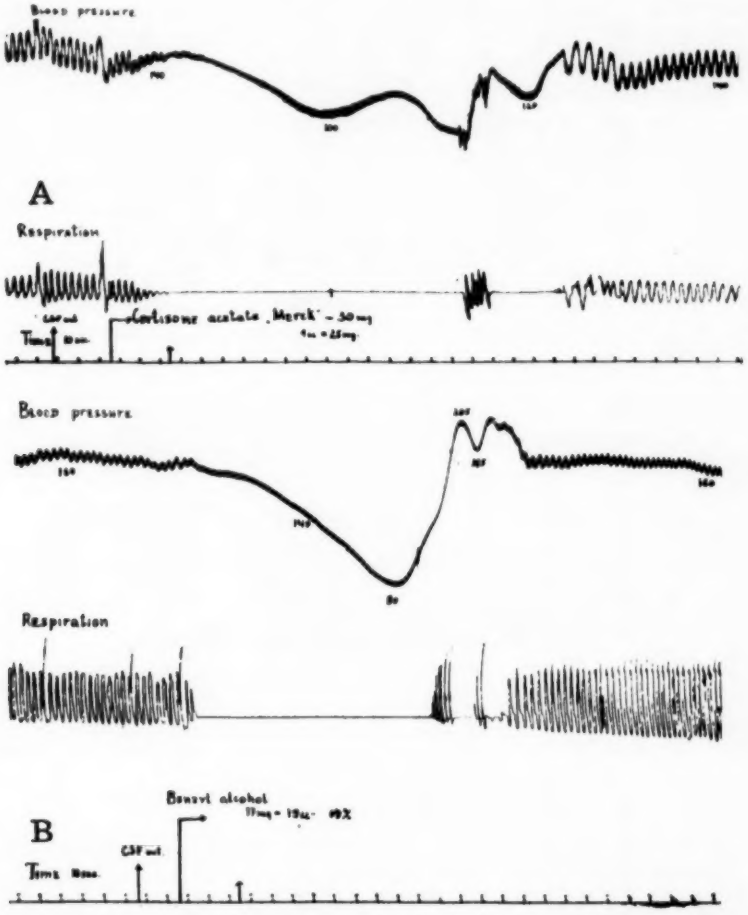

Fig. 2.—*A*, effect on blood pressure and respiration of 12.5 mg. of cortisone per kilogram of body weight (containing 4.5 mg. of benzyl alcohol per kilogram of body weight in 0.9% solution). *B*, effect on blood pressure and respiration of 4.5 mg. of benzyl alcohol per kilogram of body weight in 0.9% solution.

of isotonic saline caused a marked pleocytosis and a positive Pandy reaction after 24 hours, which lessened on subsequent days. These changes were similar to those observed after a single injection of cortisone.

2. Effect of Repeated Injections of Cortisone: In the seven cats in which repeated intracisternal injections of cortisone were made, the pleocytosis observed 48 hours

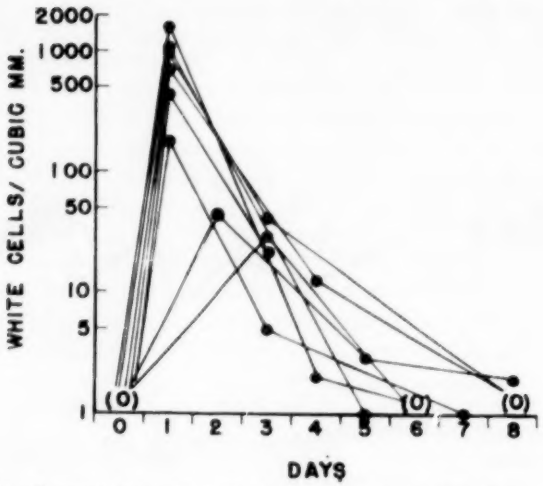

Fig. 3.—White cell counts in the C. S. F. of eight cats after a single intracisternal injection of cortisone.

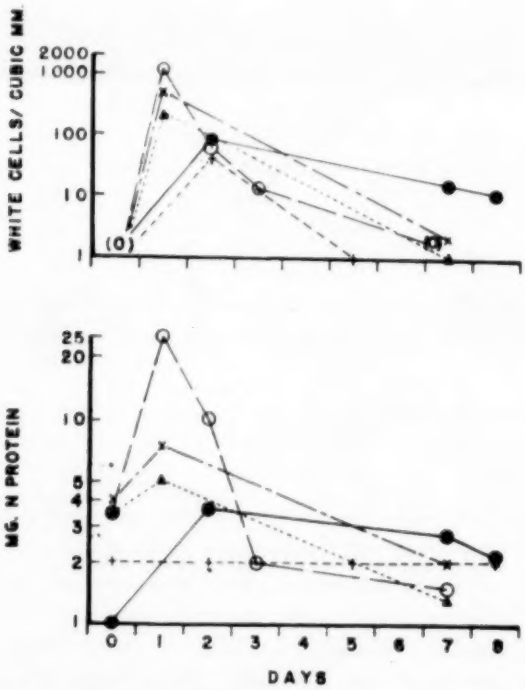

Fig. 4.—Changes in white cells and protein nitrogen in the C. S. F. of five cats after a single intracisternal injection of cortisone.

after the first injection was similar to that seen in the previous group. However, subsequent injections of cortisone did not induce the meningeal reaction observed after the first injection. In fact, in a number of animals there were no, or very few, white cells in the C. S. F. even 48 hours after a series of injections of cortisone into the cisterna magna. The changes in the white cell count are shown in Figure 5, in which every point denotes an intracisternal cortisone injection. At the time of intracisternal administration of the hormone there were no noticeable changes in the behavior of the animals. Despite the meningeal reaction following the first injection of cortisone, the cats did not show obvious neurological abnormalities.

(*c*) *Pathological Examinations.*—Examination of the brains and spinal cords of the cats used in the chronic experiments did not reveal macroscopic or microscopic abnormalities except for a few solitary perivascular aggregations of lymphocytes in the leptomeninges.

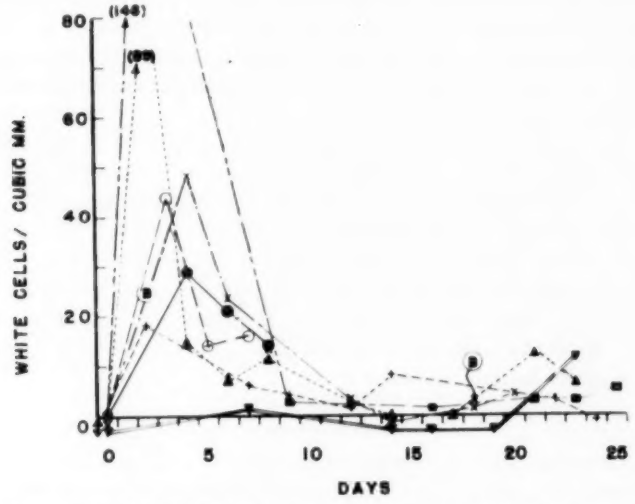

Fig. 5.—Changes in white cells in the C. S. F. of seven cats during the course of repeated intracisternal administration of cortisone. Each point denotes cortisone introduction. *B* denotes a bloody tap.

COMMENT

The results of the present study seem to indicate that cortisone acetate in doses of 1 to 2 mg. per kilogram of body weight can be safely introduced repeatedly into the cisterna magna of the cat. The meningeal reaction following a single intracisternal injection of cortisone does not differ significantly from that observed with isotonic saline. A marked pleocytosis after an intracisternal injection of isotonic sodium chloride solution in dogs has been described previously.[1] Though the injection of sterile suspensions of cortisone caused a temporary pleocytosis and elevation of protein in the cerebrospinal fluid, no exudates or adhesions were formed in the subarachnoid space even after repeated introduction of the hormone over the course of weeks. The significance of the pleocytosis following the first injection and the lack of response of the meninges to subsequent administrations of cortisone intracisternally are at present under investigation.

Benzyl alcohol, the preservative contained in cortisone acetate suspensions, seems to have a deleterious effect on the organism as a whole when introduced intracisternally in higher doses. This is shown by the changes in blood pressure, respiration, and the EEG; a similar effect was obtained with high doses of the cortisone acetate suspension. The changes in blood pressure and respiration should be attributed to the local depressant effect of benzyl alcohol in higher doses on the medullary centers. The accompanying EEG changes may have been due to the hypotension, which probably induced cerebral anoxia. In low concentrations, however, benzyl alcohol had no effect, as seen from our acute experiments with small doses of cortisone.

Cortisone is a potent drug which suppresses inflammation, inhibits the formation of fibrosis, and changes the reactivity of tissues to various noxious agents. These properties of the hormone and the fact that it can be introduced repeatedly into the subarachnoid space without any significant untoward effects may be of practical importance in experimental, as well as in clinical, medicine.

Investigations are now in progress concerning the effect of intracisternally administered cortisone and hydrocortisone on the meningeal reaction induced by talc introduced intracisternally.

While the experiments were in progress, two short reports dealing with the subarachnoid administration of cortisone appeared. Oppenheimer and Riester [2] introduced talc and hydrocortisone into the cisterna magna in two rabbits and noted some diminution in the meningeal reaction as compared with that in control animals receiving talc alone. Barnard [3] administered cortisone intrathecally in cases of tuberculous meningitis and noted that the drug exerted an anti-inflammatory action, as evidenced by the rapid return of the C. S. F. protein and cells to normal levels. As seen from his graph, there was no further pleocytosis in the C. S. F. after repeated injections of cortisone into the thecal space.

SUMMARY

Cortisone acetate was injected into the cisterna magna in cats. It was shown that 1 or 1.5 mg. of cortisone per kilogram of body weight had no effect on blood pressure, respiration, or the EEG. Higher doses caused temporary changes, which are attributable to the benzyl alcohol in the cortisone acetate suspension. A single injection of cortisone in different doses induced a transitory pleocytosis, which did not recur on repeated administration. Animals receiving cortisone intracisternally for one month did not show any significant abnormalities in the nervous system on pathological examination.

Dr. A. Behar, of the Department of Pathology, performed the pathological examinations, and Mr. J. Dobkin, of the Department of Physiology, the C. S. F. protein determinations. Mr. L. Talvi gave technical assistance.

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LOCALIZATION OF DISCHARGE IN TEMPORAL LOBE AUTOMATISM

WILLIAM FEINDEL, M.D.
AND
WILDER PENFIELD, M.D.
MONTREAL, CANADA

THE PURPOSE of the present study is to examine a recent series of cases of temporal lobe epilepsy and to localize more exactly those areas of temporal gray matter in which epileptic discharge produces automatism and its attendant amnesia. It seems evident that this study should throw some light on the fascinating subject of the mechanism of memory recording.

It is clearly established that a local discharge arising in the neighborhood of an epileptogenic lesion in one temporal lobe frequently gives rise to attacks described as automatism, uncinate fits (Hughlings Jackson [1]), or psychomotor epilepsy (Gibbs, Gibbs, and Fuster, 1948 [2]). During the attack the patient may move about, fumbling with his clothing and smacking his lips, in a state of complete confusion, resistant to reason and brooking no interference. Or, on the other hand, he may seem to be no more than slightly confused and may carry out complicated activity, showing that he has not lost all hold on memory of his past. After the attack is over, he will have amnesia for all that transpired during this period of confusion.

UNCINATE FITS

No better introduction to this subject can be made than to refer to the description of "uncinate fits" which Hughlings Jackson gave some 50 years ago, since our conclusions form a remarkable vindication of his suggestion as to localization.

Jackson proposed the following hypothesis (Jackson and Stewart, 1899 [3]): "That the discharge-lesions in these cases are made up of some cells, not of the uncinate gyrus alone, but of some cells of different parts of a region of which this gyrus is part—a very vague circumscription, I admit—the uncinate region."

Jackson noted in this "particular variety of epilepsy" the crude sensation of smell and taste with masticatory movements which appeared at the onset of the attacks. Following Jackson, other investigators have given the olfactory aura a more important place in the consideration of uncinate attacks than it deserved. Jackson himself seemed more intrigued by the dreamy states or intellectual auras characterizing many of these attacks.

Indeed, in his best-documented example of uncinate fits there was no evidence of any warning sensation of smell or taste, and no epigastric sensation was reported.

From the Department of Neurology and Neurosurgery, McGill University, and the Montreal Neurological Institute.

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Furthermore, the same case represents the only instance in his series in which the pathological lesion, as found at autopsy, was sufficiently restricted to indicate that the uncinate region was selectively involved (Jackson and Colman, 1898[4]).

The report of Jackson and Colman's patient is of great interest to the present study and may be briefly recalled. The patient was a physician who had had attacks from the age of 20 until his death, at the age of 43. Throughout this period he had kept extensive notes, which must be unsurpassed as a detailed subjective record of temporal lobe automatism and, particularly, in regard to the nuances of change in memory processes which preceded his automatic behavior.

At autopsy the brain appeared perfectly normal except in the left uncinate gyrus, where there was a patch of softening. The lesion was found on section to consist in "a small cavity, collapsed and almost empty, with indefinite walls, situated in the uncinate gyrus 5/8 inch below the surface just in front of the recurved tip of the uncus." It obviously involved or destroyed part, at least, of the amygdala (amygdaloid nucleus). The position of this cyst is shown in Figure 1, drawn from a tracing of the brain after hardening in spirit and reproduced from Jackson and Colman (1898).[4]

Fig. 1.—Reproduction of drawing which shows the site of the cyst in the uncinate gyrus, in the case of automatism reported by Jackson and Colman (1898).

From Jackson, J. H., and Colman, W. S.: Case of Epilepsy with Tasting Movements and "Dreamy State": Very Small Patch of Softening in the Left Uncinate Gyrus, Brain **21**:580-590, 1898.

There is little doubt that this case provided important evidence for Jackson's localization of the so-called uncinate attacks. He coupled this finding with the fact that Ferrier had produced masticatory movements from stimulation of this region in monkeys and concluded that similar masticatory movements in human seizures were "reflex" effects of epileptic discharge beginning in the gustatory elements of that cortical region, which, according to Ferrier, was devoted to the function of taste. Jackson did not insist on a restricted localization, however, and further noted, "Many of the symptoms of even the slight paroxysm of uncinate fits depend, of course, on discharges widespread beyond, some far beyond, the uncinate region."

PREVIOUS DISCUSSION OF AUTOMATISM

Our recent studies summarized by Penfield and Jasper (1954),[5] indicate that the dreamy states, the psychical illusions, and the hallucinations that may precede automatism are produced by discharge not in the uncinate region but in the adjacent cortex of the lateral and superior surfaces of the temporal lobe.

Penfield and Kristiansen (1951)[6] analyzed an unselected series of 222 cases of focal epilepsy in which radical operation was undertaken during a period of 11 years ending March, 1948. There were 26 patients who developed well-marked automatism during their attacks. In 2 patients the localization of epileptic discharge was considered to be frontal, and in 23 it was temporal. In one case the origin seemed to be inferior parietal or posterior temporal.

It was pointed out in a study of automatism (Penfield, 1952[7]) that epileptic discharge which arises in the classic motor area of the cortex or in one of the sensory areas outside the temporal lobe may, as the discharge spreads to subcortical areas, result in a general motor convulsion with loss of consciousness, but never producing automatism without preliminary violent explosions of movement. On the other hand, when automatism appears simply as the result of a cortical lesion, the discharge begins in the anterior frontal or the temporal region.

It was pointed out further that, judged by the pattern of the attack and the associated electrographic abnormality, anterior frontal automatism was similar in character to the petit mal seizure which is produced by subcortical discharges in the centrencephalic (or central integrating) system. Thus, although petit mal automatism, or absence, associated with 3-per-second electrographic spike-and-wave discharges, was usually centrencephalic in origin, in rare cases it was anterior frontal in origin. On the other hand, psychomotor automatism, associated with an electrographic disturbance, called psychomotor by Gibbs, Gibbs, and Lennox (1938),[8] was most frequently temporal in origin and quite possibly it, too, could be centrencephalic in origin, although recorded electrographically in both temporal or frontotemporal regions.

The common feature of these two types of automatism, petit mal and psychomotor, is the amnesia which the patient shows for the attack.

It was therefore assumed that there must exist a centrencephalic memory-recording mechanism (*A*) which could be interfered with by discharges arising in the anterior frontal cortex or the temporal cortex, and projecting thus to the centrencephalic area. Because this phenomenon occurred without producing convulsive movement or paralysis of voluntary action, it was assumed that the memory mechanism (*A*) was functionally separate from the centrencephalic motor mechanisms (*B*).

MATERIAL

The present study is based upon an analysis of cases of patients who have undergone operation with local anesthesia as treatment for their temporal lobe seizures. In a series of 155 such patients, 121 (78%) showed some evidence of behavioral automatism either at the outset of the attack or after preliminary psychical, sensory, or brief motor phenomena.

The automatism was characterized by unresponsiveness, confusion, and subsequent amnesia. Often masticatory movements were present, as though the patient were tasting something, and there were fumbling movements or unrelated speech, or inappropriate behavior, sometimes very elaborate and according to a plan, however ill-conceived it might be.

The analysis of these attacks and the identification of the various phenomena that preceded the automatism were the result of careful questioning of the patient and of those who had observed his attacks. Not infrequently such attacks were reproduced by pentylenetetrazol (Metrazol) administration during preoperative electroencephalography. The order of the phenomena was discussed and verified at conference as well.

Automatism can be produced in conscious patients by stimulation of the mesial inferior region of the temporal lobe in the same way that spontaneous epileptic discharge produces it in this zone. The behavioral automatism is present during the ictal, and immediately subsequent post-

ictal, fatigue period. During such attacks, whether they occur spontaneously or are induced by stimulation, there may be initial sudden suppression of the electroencephalographic potentials, instead of the usual exaltation of potential variations which occur in association with discharge in most other parts of the brain.

The subsequent discussion will amplify and substantiate these statements, which were presented briefly in a previous report (Feindel, Penfield, and Jasper, 1952[9]).

ANALYSIS OF SEIZURE PATTERNS

A representative sample consisting of 50 patients with temporal lobe automatism, on whom there were well-documented records, was chosen for detailed study of the seizure patterns. From this analysis it is evident that automatism may occur without being preceded by a warning. More frequently it is preceded by a single phenomenon or a succession of phenomena that occur each time before the onset of automatism and amnesia.

The localizing significance of a Jacksonian march of motor phenomena, or motor and somatic sensory phenomena, in cortical epileptic seizures has long been

TABLE 1.—*Initial Pattern of Seizures in Patients with Automatism*

	Cases
Primary automatism	
(*a*) No features preceding automatism	3
(*b*) Initial awareness of confusion preceding automatism	6
	9
Initial phenomenon in automatism preceded by one or two ictal phenomena	
(*a*) Psychical illusion	6
(*b*) Cephalic sensation	5
(*c*) Sensory features (probably second sensory)	7
(*d*) Abdominal sensation	7
	25

accepted as valid. The anatomical value of successive phenomena in temporal lobe seizures should also be recognized, for there is often an invariable succession, or march, of phenomena in such cases.

Primary or Initial Automatism.—(*a*) In a few cases nothing was reported to precede the period of automatic behavior in any of the patients' attacks. There were three such cases, as shown in Table 1.

The possibility must be considered that such a patient has a retrograde amnesia that wipes out recollection of the warning features. That this can occur seems indicated by the observation that some patients remember a warning only after brief attacks. Such attacks are observed, however, to begin in a way similar to that of severe attacks of which the patient recalls no initial warning. Or, again, the warning may be verbally reported by a patient as he goes into an attack but may not be remembered by him in the postictal period.

(*b*) In six cases the warning seemed to be an initial awareness of confusion or of difficulty in memory. The expressions offered by the patients to describe such initial features include "lack of knowledge," "difficulty in thinking," "clouding of thoughts," "hard to remember," or "things are mixed up." In one patient this was associated with blurring of vision, and in another, with tonic postural movement.

If this aura of conscious confusion is not to be interpreted as a phenomenon separate from the automatism, the six cases of that type may be added to the three in which there was no warning phenomenon, making nine examples of primary automatism (Table 1).

Further evidence for the use of the term primary automatism is provided by the production of immediate automatism, which may not be preceded by any warning features, from stimulation of a local zone of the temporal lobe exposed at operation. These responses will be described below in detail.

Automatism Preceded by One or Two Ictal Phenomena.—There were 25 patients who reported one or two initial warning features that seem independent of the succeeding automatism.

(*a*) In six patients the initial feature might be interpreted as a psychical illusion. The actual descriptions, as worded by the patients, were feelings of strangeness, dreaminess, or aloneness, or of things seeming far away or unreal. (In one patient there was an associated feeling of fullness in the throat, and in another, tonic posturing of the contralateral arm.) It may well be that these expressions identify slight nuances of mental change not dissimilar to those discussed under conscious confusion, but, in addition, the suggestion of a feeling of detachment from the patient's surroundings seems to justify the separate grouping of these phenomena as psychical illusions. One patient of this group had a feeling of fear, along with numbness of the contralateral hand, preceding the automatic behavior.

(*b*) Five patients reported a cephalic aura, which was described as a strange feeling, or a lightness, a dizziness or warmness in the head. This sensation was associated in two patients with a feeling in the chest, and in a third patient it was followed by turning of the head before the onset of automatism. These phenomena also should be compared with the expressions discussed above. In one patient of this group there appeared to be a sensation of true headache.

(*c*) In seven patients the features occurring before the automatism were sensory in nature and of a quality suggesting discharge involving the second sensory cortex deep within the Sylvian fissure. One patient reported that he felt cold all over his body and had a little dream. Another had a "feeling of uneasiness" beginning in the contralateral arm and chest, then involving the whole body, and associated with slight stiffening and tremor of the arm. Another had a vague sensation, together with a trembling in the entire contralateral side of the body, preceding the automatism. Still another complained of "painful spots" on his tongue. In three additional patients the initial phenomena preceded the automatism as follows: sudden sensation in the ear and stiffening of the hand; feeling in the scrotum and forced thinking; and sensation in the hand with difficulty in drinking and swallowing.

(*d*) Three patients remembered an abdominal sensation before going into an attack of automatism. In two it was associated with inability to speak. Four other patients had initial epigastric sensation associated with a dizzy sensation, vocalization, stiffening of the arms, or blurring of vision, respectively.

Automatism Preceded by a Succession of Ictal Phenomena.—In the remaining 16 of the 50 cases selected for analysis, multiple features, from three to five in number, presented in the seizure pattern before the appearance of automatism. It

is of interest that of these 16 patients, 8 had abdominal sensation usually at the beginning of their attack, and in 4 of these patients this was also associated with a feeling of fear.

The incidence of various phenomena preceding automatism in all 50 cases, regardless of whether they occurred alone or in sequence with other ictal phenomena, is listed in Table 2. Brief comments may be made on the more frequently occurring of these phenomena. It is evident that there is a striking predominance of phenomena having a sensory quality. Of these, abdominal sensation is the commonest. In all instances in which this occurred, it came as the very first feature of the attack, although in two cases there was a feeling of intestinal movement, which did not occur at the onset of a warning sequence. Furthermore, abdominal or epigastric

TABLE 2.—*Incidence of Phenomena Preceding Automatism in Fifty Patients**

Abdominal sensation (includes nausea)	17
Conscious confusion	16
Tonic or adversive motor features	12
Sensation, except abdominal and cephalic	11
Cephalic sensation	9
Dreamy, far-away, unreal feeling	9
Blurring of vision	8
Fear	7
Flushing of face observed	6
Pallor of face observed	5
Difficulty in speaking	4
Auditory illusion or hallucination	4
Visual hallucination	4
Micturition or desire to void	4
Drowsiness	3
Praying or religious expletive	3
Scrotal sensation	2
Olfactory illusion and hallucination, of each	1
Taste, lacrimation, perspiring, dyspnea, vertigo, awareness of borborygmi, awareness of intestinal movement, pounding of heart, difficulty in swallowing and breathing, of each	1

* Thirty-six patients had more than one feature.

aura is almost never succeeded immediately by automatism, other features being interposed in the seizure sequence before automatism.

Conscious confusion, as referred to above, also occurs frequently. It presents in only two positions in the seizure sequence, either immediately preceding automatism or separated from automatism only by tonic or adversive motor phenomena. In all 12 instances in which tonic or adversive motor phenomena were present, they occurred immediately before automatic behavior. Conscious confusion followed by tonic or adversive motor features therefore constitutes a common epileptic "march" leading into automatism. Such movements were usually of mild degree, and the duration of the automatism which followed was out of keeping with the briefness of the motor phase. It is thus clearly differentiated from the postictal automatism following a generalized motor seizure. It is of significance that both these phenomena, the conscious confusion and motor features, have been produced by stimulation of the brain, as will be noted below.

However, a variety of other phenomena appeared less commonly before automatism in the seizure pattern, their sequential arrangement showing considerable

variation, and an understanding of their pattern awaits further study of the physiology of the temporoinsular region. In addition to the visual, auditory, and psychical phenomena, note should be made of the various autonomic effects.

It should be emphasized that olfactory sensation was reported in only two patients, and a sensation of taste in only one patient, of the entire group. Clinical evidence would thus suggest that the true olfactory system has not a very common relationship to the neural structures involved in automatism. Masticatory movements, salivation, and swallowing were reported or observed as an accompaniment of the automatism in half of the cases. We have tended to include these as a manifestation of automatic behavior (Magnus, Penfield, and Jasper, 1952 [10]).

PRODUCTION OF AUTOMATISM BY STIMULATION

Stimulation of the brain during operation in patients given local anesthesia has produced automatism and amnesia, and this may be associated with suppression of the brain potentials as recorded in the electrocorticogram. The foregoing statements are illustrated by the following cases.

Stimulation of the Amygdaloid Region.

CASE 1.—P. S.,* referred by Dr. Henri Hécaen, Paris.

This man, aged 26, had a history of difficult birth, necessitating the use of forceps. From the age of 12 onward, he had had attacks which began with a vision of colored lights, or a feeling which he described as a "shock in the head" or "lack of knowledge." He then became unresponsive and fumbled with his clothes or with objects he was holding. Occasionally he had an attack for which he remembered no warning. He would never remember his actions during the period of automatic behavior.

In addition, he had longer periods of peculiar behavior. For example, while in hospital his anticonvulsive medication was withdrawn. This resulted in an increase in minor seizures and a continuing peculiarity of behavior. He reported visual or auditory hallucinations and dreams that he was in heaven and could see colored saints. The condition cleared up when the drugs were given again.

Roentgenological findings indicated smallness of the right side of the skull, with enlargement of the lateral ventricle on the right. Electroencephalographic study showed abnormal spike activity over the lateral and inferior temporal regions. During a seizure the record showed initial suppression of the spike discharges, followed by 6-per-second rhythmic waves over the right frontotemporal region.

At operation, the right temporal region was exposed, with the patient under local anesthesia. Attempts to reproduce his aura by various electrical stimulations in the lower central cortex and deep in the lateral and posterior temporal regions failed.

A typical attack, however, was produced by stimulations more anteriorly at Point *17*, deep to the second temporal convolution, using an electrode that was coated except at the tip. The position of the stimulation site (Fig. 2), as shown on a coronal section of the hemisphere, lay in the temporoinsular sulcus, between the superior and the mesial surface of the temporal lobe. Recording electrodes had been placed over a wide area of the temporal cortex.

At the close of stimulation, the electrographic background activity and the spikes which had been present previously were found to have been replaced by low-voltage activity over the entire temporal region, with rapid waves particularly from the region of what had been before stimulation the spike focus (Fig. 3). At the same time, the patient made a sudden brief movement of his body, then was seen to stare and become unresponsive to questioning, while he made plucking

* The case of this patient was also described from certain points of view by Penfield and Jasper (1954).[5] See P. Sa. in the Case Index.

movements at the anesthetist's coat. He pulled his arm away roughly, as though not wanting to have it held. He made intermittent chewing movements, and his whole appearance was that seen previously in his habitual attacks.

The poststimulation electrographic suppression was interrupted by a brief rhythmic discharge, followed in turn by a second suppression or flattening of the record, and the automatic behavior continued all the while.

With return of the spike activity (*95 sec.*, Fig. 3), the patient appeared to have recovered from the attack. Immediately on recovery he did not seem to be aware that he had had an

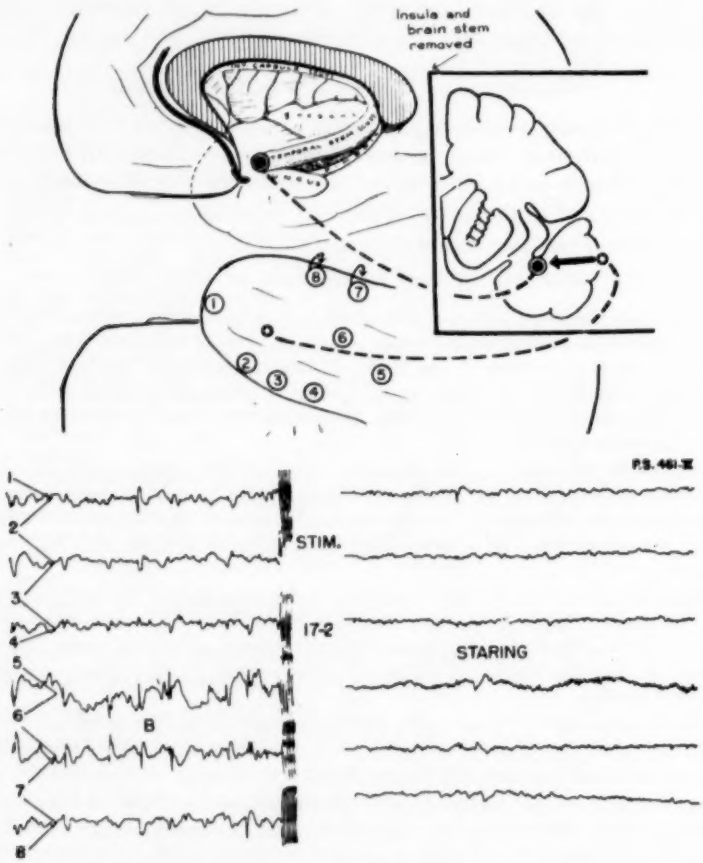

Fig. 2 (Case 1).—Diagram to show the site of deep stimulation (indicated by the target circle). The numbers show the positions of recording electrodes and corresponding channels on the electrocorticogram. Note the flattening of the record and cessation of spike activity following stimulation.

attack. Later, he said he knew because something "ran through his cranium." At 50 seconds the electrographic record seemed to be characteristic of postictal flattening, but it is noteworthy that the automatic behavior continued through this period unchanged.

The right temporal lobe was removed, but abnormal spike discharges were still found in the cortex of the orbital operculum. Removal of abnormal cortex in this area was followed by

improvement in the electrocorticogram. A postoperative electroencephalogram, taken two weeks later, showed no spike activity and no delta waves.

It is now three years after operation, and the patient has had no attacks. But also of interest is the change reported in his behavior. Previous to operation he had been considered a little strange and ineffectual, though intelligent. His father had described him as *un peu mystique*. About one year after the son's operation the father died, and the patient has ably taken over responsibility for the family affairs and has done it well, an achievement that would not have been expected of him by his family and friends before operation.

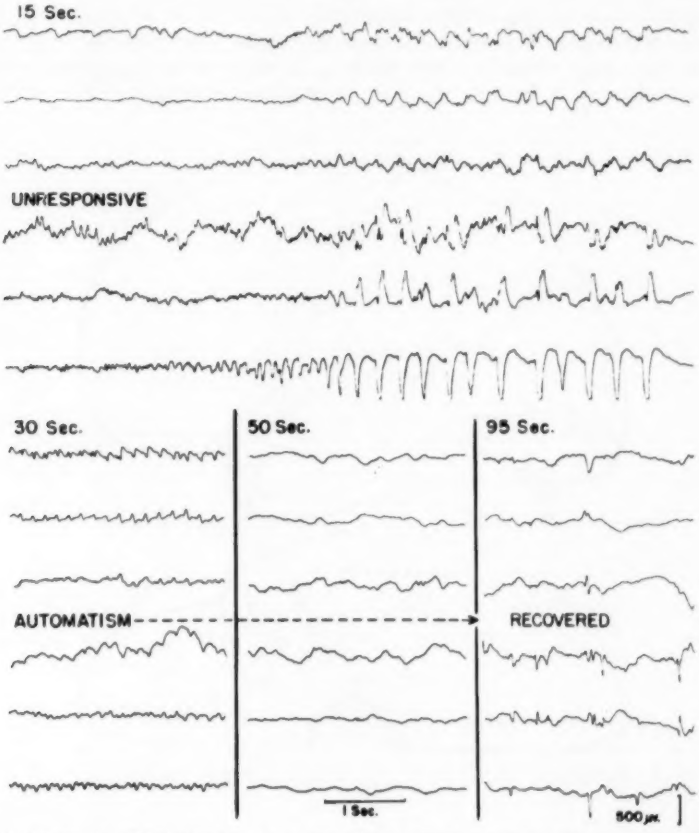

Fig. 3 (Case 1).—Continuation of the recording in Figure 2. The patient continued to have automatism during the after-discharge and second period of low-voltage activity. Note the return of spike activity after 95 seconds.

The pathological changes consisted in smallness and toughness of the first temporal and hippocampal gyri. A zone of abnormal gelatinoid tissue, about the size of a small walnut, was located deep in the temporal lobe, lateral and inferior to the ventricle. This abnormal tissue is shown by cross hatching in Figure 4. Its proximity to the hippocampal gyrus and the amygdala should be noted. There was no evidence of displacement due to this tissue. Microscopically, it showed dense astrocytic gliosis, with vacuolation of the background tissue.

In summary, the distribution of the abnormality of the brain in this case was consistent with the view that it was due to head compression at the time of birth

causing herniation through the incisura of the tentorium and temporary occlusion of the arteries of the inferior and mesial surface of the temporal lobe and extending a little way into the under surface of the frontal lobe.†

In this instance automatism was clearly produced by electrical stimulation deep within the temporal lobe near the sclerotic lesion, and the behavioral and electrographic evolution of the attack was recorded. The patient's actions were those of his minor seizures. The electrocorticogram, shown in Figures 2 and 3, showed spike activity at *B*, on the anterior and lateral surface of the lobe. After stimulation there was suppression of potentials, followed by active discharge and succeeded, in turn, by flattening of the record. With the return of the patient to a normal behavioral state, at 95 seconds, the spike discharges reappeared.

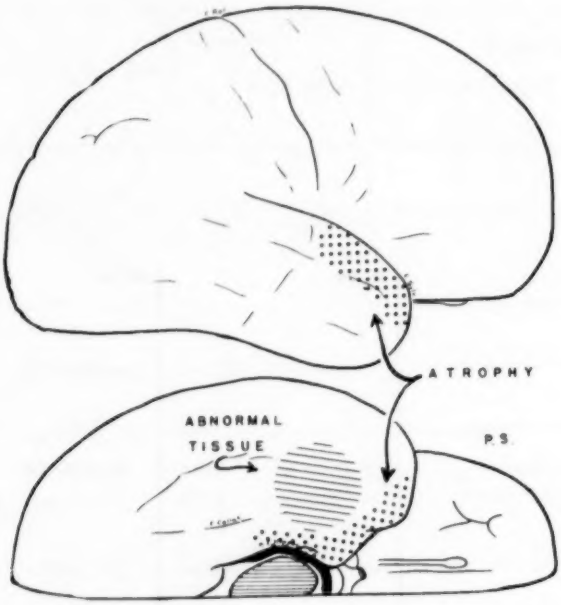

Fig. 4 (Case 1).—Area of gross atrophy and of abnormal tissue.

Thus, the automatic state which was produced by stimulation was present during electrical discharge and after cessation of this discharge; it was ictal and postictal.

Further examples of the production of automatism by stimulation in patients during operation under local anesthesia will be presented briefly. The extracts are quoted from records dictated by the surgeon during the operation after consultation with those who observed the patient and with Dr. Jasper, who made the electrocorticogram. The automatism, as will be seen, was characterized by confu-

† This case was a very marked example of incisural sclerosis. The histological changes are described by Earle, Baldwin, and Penfield (1953) and material from this case (P. S.) is pictured in Figure 2*E* and *F*.[21]

sion, fumbling movements, chewing and swallowing, unresponsiveness to questions, and inappropriate speech. The patient had subsequent amnesia for the period of automatism, although occasionally he could remember some initial phenomenon.

CASE 2.—J. O. Stimulation was carried out in the left uncinate region.

"The patient slapped with his right hand. He said he felt pressure and smelled something, but this passed off without an attack. When asked what it had smelled like, he said, 'like a chicken in a chicken coop.' Stimulation was then repeated 1 cm. anteriorly, still in the uncinate region. Patient said, 'Oh, brother!' Then he seemed to go into an attack; his eyes stared, and he moved his hands as before, and began to masticate. After about a minute or two he spoke: 'I rang a bell; I wanted to speak to Bill.' When asked, he explained that 'Bill was working for the Mayor,' and then he corrected this to 'the King.' After the attack was over, he was unable to recall any warning, olfactory or otherwise."

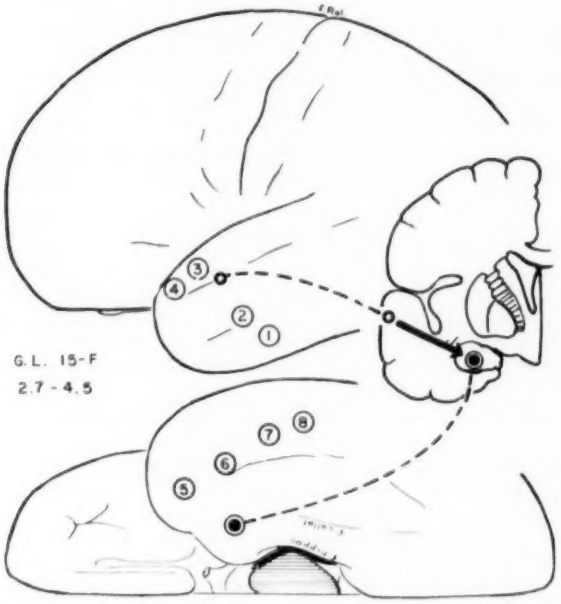

Fig. 5 (Case 4).—Diagram to show site of deep stimulation. The numbers indicate the positions of recording electrodes. There was flattening of the record from the anteroinferior surface of the temporal lobe.

This was reproduction of fumbling movements, mastication, and inappropriate speech with complete amnesia for the period, as the result of stimulation of the uncinate region.

CASE 3.—A somewhat similar response with amnesia was obtained in Patient J. R. "Stimulation 3.5 cm. from the temporal pole and about 3 cm. deep in the second temporal convolution caused the patient to fail to respond except by grunting. He then seemed to move both hands, making a fist with each hand, opening and closing. Following that there was after-discharge on the electrocorticogram. At the end of this after-discharge the patient was still confused. His eyes were open and looking about. Just before the after-discharge disappeared there was mastication. When asked how he was feeling, he said: 'I am feeling well. How are you?' Later, when asked, the patient said he did not know he had had an attack and he did not remember going into one. The region of stimulation was near that stimulated in Case 1."

CASE 4.—Further evidence that deep structures within the temporal lobe are concerned with attacks of automatism is given in the case of G. L., a woman of 29. Since the age of 20, she had

had seizures which began with a dream, "a familiar feeling," a "drifting away," and continued with staring, unresponsiveness, chewing movements, and smacking movement of the lips, followed by talking at great length and fumbling.

Left temporal craniotomy was carried out. Stimulation deep in the anterior temporal region with the coated electrode reproduced various features of her seizure. The sites of stimulation producing positive responses fell in a region between the temporoinsular groove and the uncinate surface of the temporal lobe. One example is given from the operation record.

"Deep stimulation 4.5 cm. straight in from the first temporal convolution was carried out, attempting to place the electrode in the uncus [Fig. 5]. It was observed that the patient did not respond. There seemed to be a little change in pulse rate, and there was mastication and swallowing. There was some flattening of the electrical activity observed from recording electrodes placed on the anteroinferior surface of the temporal lobe. This flattening was followed by afterdischarge at Point *6* and then a 3-per-second discharge appearing on the inferior surface and spreading to the lateral surface of the temporal lobe. Then the patient began to talk, at first repeating everything the observer said, and then talking nonsense."

Placement of the electrode, in a dissection of the temporal lobe, using the same directions and measurements as at operation, showed that the tip was directed into the region of the amygdala. The site of the electrode in such instances is not to be taken as exact. More precise localization can only be confirmed by stimulation during removal of the temporal pole, when the amygdala and hippocampus are directly visualized (Cases 6, 8, 9, 10, and 11).

Case 5.—In another patient, F. D., deep stimulation in the right temporal lobe produced a mild episode that might be described as automatism or confusion with a definite disturbance in memory.

Stimulation was carried out at a depth of 2.5 cm., with the tip of the electrode approximately beneath the insula. The patient said first, "It hurts." The electrode was then withdrawn a little. The patient seemed to try to reply but did not do so. There were some repetitive movements of the lips. He seemed a little confused, as judged by the movement of his hands. Then he said earnestly, *"Je suis malade."* Then he seemed to describe something which was difficult to understand but ended by the exclamation: "I seem to lose my memory." Dr. Pasquet, who was talking with the patient after this confusion, observed that he failed to remember some of the things he had said during or at the close of the stimulus.

Case 6.—A vague warning sensation which seemed to be related to his head, together with confusion and irrelevant speech, was produced in another patient (A. J.) by stimulation of the temporal gray matter deep in the anterior part of the Sylvian fissure.

Stimulation at a point on the medial surface of the temporal lobe where it lies against the insula caused the patient to say, "Slightly like going into a trance." When asked if it felt like an attack, he said, "It would have been, but I did not have the chance to inform you." After removal of the anterior temporal lobe 4 cm. back from the tip, the ventricle having been opened, further points were stimulated. Application of the electrode to the cortex on the undersurface of the temporal lobe caused the patient to say, "Time and space seem occupied." Then he added, "It might have been one of those seizures, and it might not." When this stimulus was repeated, the patient spoke of a sensation in his head. Stimulation of the gray matter on the posterior and inferior margin of the insula, adjacent to the largest branch of the middle cerebral artery, caused the patient to say that he "was all mixed up" and that he "could not get his thoughts straight."

Case 7.—A remarkable example of confusion, amnesia, and irrelevant rambling speech was recorded in the case of J. G. After removal of the anterior part of the left temporal lobe, stimulation in the gray matter on the cut surface inferiorly, near the uncus, gave the following results.

The patient reported a sensation in the eye and then said, "I saw double." A little later he said, "I put the thermometer in my suitcase." When asked if he had had a dream, he said, "Well, it might be." He then talked in a confused manner.

Stimulation at Point *19*, just posterior to Point *18*, caused the patient to say, "Yes." Then he said something about a mountain in New Jersey and about driving a car, and appeared confused. Further examples of what the patient said during his period of confusion were as follows: "I do not know where the food goes on the left hand side." "It is a good thing to have your flags to throw away; to have your clags, your own clags to give away." "You should have taken a half

box of that Canadacca paint, and you would have been able to paint." "Did they put that hotel away, the one with the name on the back of the matches?" There was hesitation and apparent difficulty in word finding during this period of confusion, suggesting some involvement of speech mechanism.

CASE 8.—In Patient M. S., after removal of the anterior end of the left temporal lobe, stimulation of the cut surface of the uncinate region gave similar responses of delirious or irrelevant speech. On stimulation, 1 cm. deep in the first temporal convolution, the patient replied, "Kind of sick." These are the words she used to describe her aura. The stimulus was repeated, with the same result. On stimulation of the uncus, the patient said, "That's a cement, kind of . . ." The sentence was unfinished, but she repeated something about cement several times. This resembled her speech during the automatic behavior of her minor seizures. A subsequent stimulation carried out on the uncus more posteriorly produced complete arrest of respiration. This stimulation was repeated, and respiration stopped for about 30 seconds. Dr. Kaada then spoke to her, and she replied, "You wash clothes at home."

CASE 9.—This patient (R. M.), 31 years of age, had been having seizures with automatism from the age of 19. His attacks began with a feeling of drawing up of the scrotum. This was then followed by what he described as a change in his thoughts, although he could give no further description of what he meant by this. On some occasions he seemed to be aware of confusion at the beginning of the attacks. He recalled an instance when he was typing and continued to type. He was then aware of his hands stopping and observed that the typing he had just done made no sense. Others had observed him repeating the same word over and over again during such episodes. He had one attack when he remembered that he had sat down in a bus and next found himself at home, but unable to fit the key into his door lock.

At operation there was found marked induration, yellowing, and atrophy of the left first temporal convolution, uncus, and hippocampus.

Vague warnings of his attacks were reproduced by stimulation on the lateral temporal cortex, but stimulation deep in the temporal lobe produced visual hallucinations which were noted by the patient to correspond to what he meant by a "change in his thoughts." Deep stimulation also caused the patient to become unresponsive and to make irrelevant repetitive remarks, for which he was amnesic afterward.

During one of the deep stimulations the patient said, "O God, watch over me," and repeated this several times. When asked, after the stimulation was over, what he had said, he apparently could not remember.

The whole procedure was repeated, but without introducing the electrode, and the patient replied "No" to all questions.

Stimulation after an interval of 10 or 15 minutes produced, again, the same response on two occasions. Each time the patient made pleading prayerful remarks but after the stimulation had no recollection of having said them.

During excision of the temporal cortex, the gray matter was exposed at the point where the temporal cortex joins the insula. Stimulation here, just anterior to the temporal horn of the ventricle, in a site which was judged to correspond to the region previously stimulated by the deep electrode, caused the patient to be confused during conversation. He mumbled and did not answer properly to ordinary questions.

The electrocorticogram showed the presence of active spike discharges when recording electrodes were placed in this region. Deep stimulation more anteriorly in the temporal pole had failed to produce any features of his attacks.

Stimulation of the Insular Cortex.—Electrical stimulation of the gray matter of the insula, as it lies in the depth of the temporoinsular fissure, has yielded similar responses. An example follows.

CASE 10.—C. E. This patient complained of minor attacks ushered in by a feeling of coldness all over his body and, sometimes, nausea. Automatism and amnesia were produced by stimulation in the gray matter at the junction of the right anterior insula and the temporal lobe.

When this area was first stimulated, he said, "Will you keep that up for a little while; I feel awful like an attack." The electrode was kept in place. "I had the nausea and then that feeling all over; it is hard to describe." The patient then reached up with his left hand in a rather

energetic manner, manipulating the drapes and bar (of the operating table). Dr. Roberts, who was observing him, said that before the patient reached up to the drapes, he had carried out fumbling movements with his left hand. When asked, the patient said he did not remember reaching up. It was apparent that he had amnesia covering a brief period.

Stimulation was repeated without warning and kept on for 20 seconds. At the time of this unannounced stimulation he began to open and close the fingers of both hands. Dr. Roberts asked him if he was going to have an attack. The patient reached up to the drapes and said, "Get this thing off"; then he said "Is the operation over?" After that Dr. Roberts said, "How are you?" and the patient replied, "I am having that cold feeling now." When asked where the cold feeling was now, he said, "I can't remember any more." When asked, he said he did not remember moving his hands, but he remembered asking about the operation being over.

This case report illustrates how a patient may emerge from the period of amnesia. His request that the surgical drapes should be removed showed a failure to understand the present situation. With the return of ability to record memory

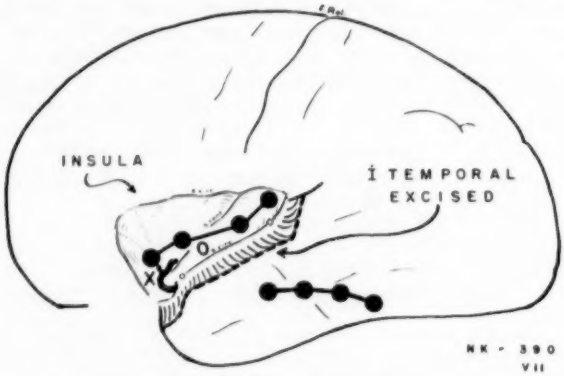

Fig. 6 (Case 11).—Diagram to show position of electrodes and sites of stimulation at *X* and *O* on the insular cortex, after removal of the first temporal convolution.

of the present situation, he asked a reasonable question "Is the operation over?" He was conscious during the period of amnesia, but understanding was limited.

There was suppression of spike activity in the electrocorticogram during the period of confusion.

Case 11.—In another patient, N. K., attacks began with a sudden feeling of fear, followed by an automatic state in which there was vocalization and staring, followed by fumbling motions and mastication.

A left temporal craniotomy was carried out, and the first temporal convolution was removed (Fig. 6). Electrical recordings were then made from the remaining temporal lobe and from the insula thus exposed. In the midportion of the insula stimulation gave negative results. In the anterior insula stimulation repeatedly produced the feeling of fear, which the patient reported to be like going into an attack.

The electrocorticogram showed active spike discharge from the surface of the insula (Fig. 7). This was unaffected by the negative stimulations but was suppressed for about 40 seconds following the stimulation which produced her aura of fear.‡

‡ In this case the slow waves from an acute lesion of the lateral surface of the temporal lobe were not affected by the suppression.

In this example the aura which ordinarily preceded the patient's automatism and amnesia was reproduced. One may assume that a further spread of discharge from the insular cortex into the amygdaloid region would have produced the automatism.

Stimulation Producing Automatism and Tonic Motor Responses.

CASE 12.—J. R., aged 28, referred by Dr. Frederick Bush, West Bend, Wis.

This man had suffered from attacks, beginning at the age of 2 years. The preoperative summary of the attack pattern was as follows: (1) cephalic aura; (2) hand sensation; (3) tonic stiffening of extremities and body; (4) automatism; (5) major tonic-clonic seizure.

There was electroencephalographic localization of an epileptogenic process in the left temporal region. X-ray examination showed that the left middle fossa was shallow and small and that

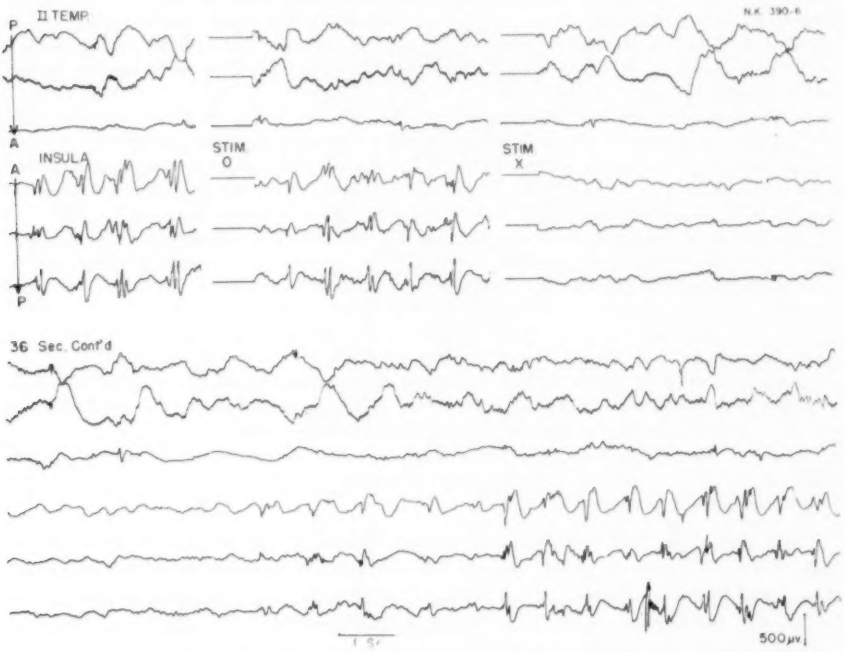

Fig. 7 (Case 11).—Electrocorticogram, showing the record from the temporal lobe (P to A), and from the insula (A to P). Stimulation at O gave no change. Stimulation at X was followed by a flat record, with arrest of spike activity and production of the patient's aura.

the inferior horn of the left lateral ventricle was a little enlarged at the tip. The preoperative diagnosis was focal cerebral seizures, probably due to birth compression and, secondarily, to an epileptogenic lesion in the inferior and mesial portion of the left temporal lobe.

There might be a prodrome of what he called a small headache. The attack itself began with a sensation in the posterior vertex of the head. This was described as a tightening sensation, which became more intense and was followed by a feeling of tightening in the right hand. During that time the patient felt that he could understand what people might be saying to him. This phase was followed by what the patient thinks was movement of his right hand and spread as a sensation to his whole body. He added that he had learned to carry his cigarette in his left hand so that he would be able to put it out at the beginning of a seizure.

The father described the attacks as follows: The boy stared for 10 to 15 seconds; he looked at his father but did not reply and showed no evidence of understanding. He would resist any

interference. Then he stiffened and fell to the floor, after which the father thinks there was some shaking, but after that the boy got up and moved about in an automatic manner.

In an attack which was observed while in hospital, this period of resistance and confusion was followed, after a minute or two, by turning of the head and eyes to the right and clonic movements of all extremities, lasting approximately three minutes, with cyanosis and biting of the tongue depressor. After that he began to slap himself over the abdomen and chest alternately and to kick with his left leg in an aimless fashion. This state was followed by a lack of response for about five minutes, after which he was able to name objects without evidence of aphasia, but was unable to remember anything that had happened just before the attack. Later on he was able to recall the onset of the seizure.

Small attacks of this same pattern were produced by deep stimulation in the left temporal lobe at the time of operation, with the electrode directed toward the uncus. This stimulation caused the patient to have a tightening sensation in his right hand, flexion of the wrist and fingers, and actual stiffening of the arm. For a brief period it was found that he could not count the observer's fingers. During this time one finger of his right hand was pinched, but he did not seem to remember it afterward. When asked about the attack, he said he seemed to lose control of his thoughts for a minute.

After removal of the anterior end of the temporal lobe, it was possible to stimulate the amygdaloid region and the hippocampus separately. Stimulation of the amygdaloid gray matter caused the patient to have an attack; his right arm became stiff, the wrist flexed, and the hand closed. His mouth pulled to the right. When asked, he said he had had some feeling in his head and his hand, also in his face. "Yes," he said, "that was like a seizure."

Stimulation of the hippocampus alone caused him to say that he felt something on the right side of his mouth. Stimulation after introduction of the electrode 3 to 5 mm. into the amygdaloid gray matter caused the patient to flex and stiffen his arm, pull his mouth to the right, and extend the right leg. He said it felt very much like an attack. After sucking out the amygdaloid nucleus, stimulation of the white matter superior to it produced a movement of the arm which was similar to, but less marked than, that described above.

Some of these brief attacks were accompanied by temporary arrest of the spike discharges recorded on the electrocorticogram. In discussion, following operation, the patient stated that the small attacks produced by stimulation were like his habitual seizures.

In this instance (Case J. R.), in addition to the impaired state of consciousness and amnesia, stimulation of the amygdaloid region produced a sensation of tightness and actual tonic posture of the contralateral extremities.

We should hesitate to conclude from this evidence that the hippocampal gyrus has of itself a motor function or that the amygdaloid and hippocampal areas are devoted to bodily sensation. Nevertheless, stimulation there produced sensation and stiffening movement, as well as amnesia and interference with consciousness. Immediately subsequent removal of these structures did not produce loss of sensation, interference with conscious processes, or paralysis. It might therefore be surmised that adjacent subcortical structures, such as those in the basal ganglia and thalamus or brain stem, were being played upon by direct neuronal bombardment during the spontaneous, as well as the induced, attacks.

Summary of Stimulation Results.—Figure 8 shows the sites of stimulation producing automatism in 16 patients. The open circles indicate stimulation on the surface. The target circles indicate sites of deep stimulation as they were visualized later on the cut surface of the temporal lobe or located by measurement of the depth of the electrode and its distance from the temporal tip.

Nineteen of the 25 responses obtained in these 16 patients lie in the mesial temporoinsular gray matter and in the area about the amygdaloid nucleus. It should be noted that in our experience automatism has never been produced from stimulation of the tip of the temporal lobe.

Numerous stimulations in other parts of the temporal lobe or in other cortical regions failed to produce automatism, except in the rare instances which are indicated in the brain chart shown in Figure 8.

Confusion and automatic behavior did follow stimulation at the site of the circles on the surface of the first and second temporal convolutions and the posterior Sylvian region (Fig. 8), but in each of these three instances the discharging

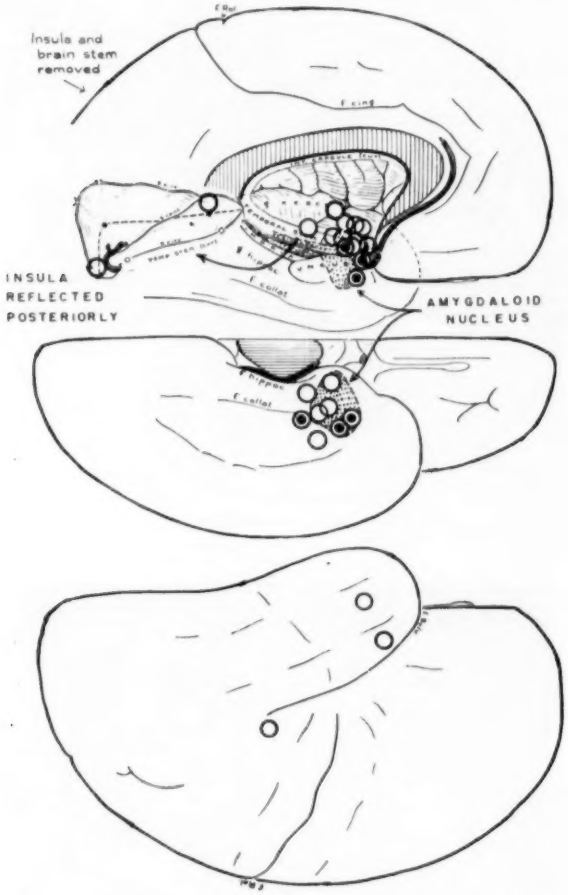

Fig. 8.—Sites of stimulation producing features of automatism in 16 patients. Open circles indicate surface stimulation, and target circles indicate deep stimulation.

focus was shown to be deep in the Sylvian fissure and spontaneous seizures were occurring. It was concluded that the responses had no reliable localizing value.

Electrographic Suppression.—A particularly interesting feature of some of these attacks is the initial sudden suppression of the EEG record. Thus, the background activity and such spike potentials as may be present are replaced by low-voltage rapid waves, or simply by low-voltage activity. This electrographic suppression

may be generalized or bitemporal in distribution, or, rarely, it may be confined to the temporal region of one side. The rapid involvement of the entire temporal lobe, often bilaterally, during these attacks is worthy of note. Automatic behavior

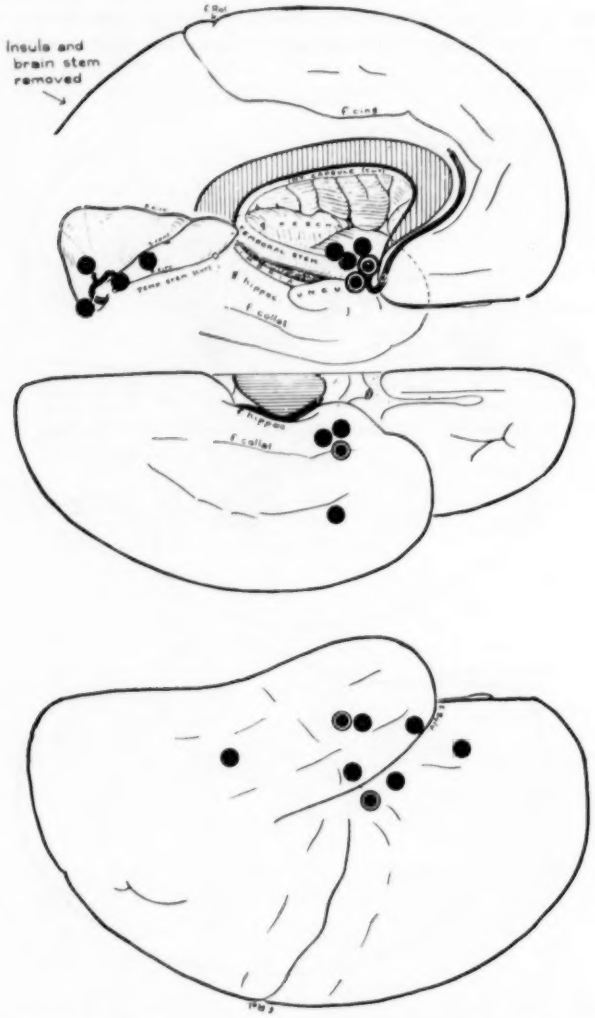

Fig. 9.—Sites of stimulation producing suppression of electrical activity. Solid circles are points of surface stimulation, and target circles are points of deep stimulation.

may follow immediately on a brief period of suppression, or it may parallel a more prolonged period of low-voltage activity (Case 1, Figs. 2 and 3).

Figure 9 shows the sites of stimulations which were followed by suppression of electrical activity on the corticogram. Surface stimulations are indicated by solid circles, and deep stimulation by target circles. There are 21 stimulation points

collected from 16 different patients. Thirteen points are located in the mesial temporoinsular region, and stimulation at 10 of these points resulted in suppression associated with automatism. It is evident, however, that electrographic suppression can also follow stimulation of the lateral surface of the temporofrontal cortex, but in none of these instances was the suppression associated with automatism.

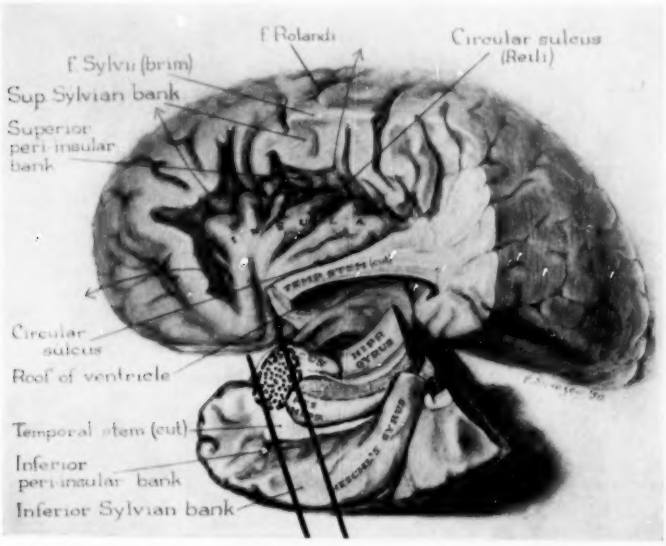

Fig. 10.—Dissection with the temporal lobe laid aside. The position of the amygdala is indicated by stippling. The two black lines are 3 and 5 cm., respectively, from the tip of the temporal lobe.

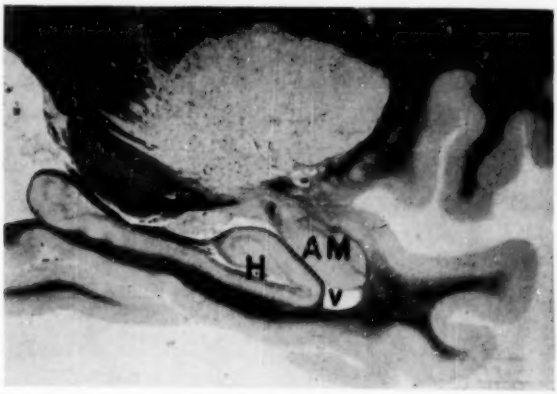

Fig. 11.—Sagittal section through the temporal lobe, showing the relation of the amygdala (*AM*) to the hippocampus (*H*) and to the temporal horn of the lateral ventricle (*V*).

COMMENT

Anatomy of the Periamygdaloid Region.—The mesial temporal region from which automatism can be produced lies at the junction of the frontal, insular, and temporal cortex (Fig. 10). It seems to center about the amygdaloid nucleus and

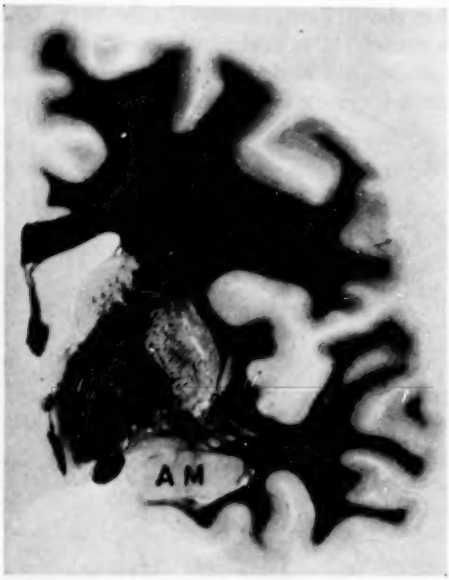

Fig. 12.—Coronal section of cerebral hemisphere, taken through the amygdala (*AM*) at 4 cm. from the temporal tip.

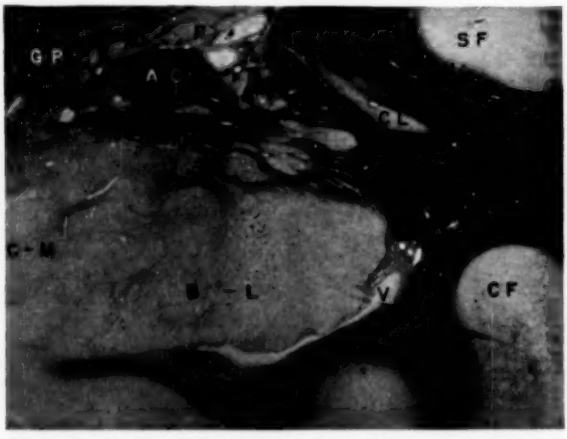

Fig. 13.—Enlargement of the amygdaloid region from the previous coronal section. The basolateral nuclear groups (*BL*) and the corticomedial nuclei (*CM*) are shown in relation to the tip of the temporal horn of the lateral ventricle (*V*). The tip of the hippocampus (*H*) is seen in the ventricle. Other structures shown are the claustrum (*CL*), anterior commissure (*AC*), globus pallidus (*GP*), and putamen (*P*). The base of the Sylvian fissure (*SF*) and the collateral fissure (*CF*) are also seen.

would include the ventral part of the claustrum. The amygdaloid nucleus, indicated by stippling, lying deep to the uncus, is situated anterior and medial to the temporal horn of the ventricle. It begins 3 cm. behind the temporal pole and extends posteriorly for another 2 cm., its posterior part overlapping the anterior hippocampus. This relationship is shown in a sagittal section taken through the temporal lobe (Fig. 11). In coronal section the amygdaloid nucleus is clearly seen in relation to the uncus and to the insular and temporal cortex (Fig. 12).

At higher magnification the division of this conspicuous mass of gray matter into nuclear subgroups is evident (Fig. 13). In primates only the medial nuclear groups appear to receive direct projection from the olfactory tract (Meyer and Allison, 1949 [11]). It should be emphasized that the exact anatomical connections of the basolateral nuclear groups are not yet known, although it is precisely these nuclei which are highly developed in primates and which may be largely non-

Fig. 14.—Enlarged view of the anterior junction of the temporal lobe and the insula. Note the compact fiber bundle at the bottom of the Sylvian fissure (*SF*) and the direction of its fibers through the gray islands of the ventral claustrum (*VCL*).

olfactory in function. They are related by way of the stria terminalis to the anterior hypothalamic and septal nuclei and are contiguous posteriorly with the tail of the caudate nucleus.

In a coronal section taken more anteriorly (Fig. 14), at the anterior junction of the temporal and the insular cortex, a striking feature is the appearance of a compact fiber bundle (which apparently belongs to the uncinate fasciculus). This lies in the temporoinsular cortical gray matter. Some of its fibers can be traced into the superficial layers of the neighboring insular and temporal cortex. The deep portion of this bundle joins the uncinate fasciculus, which sweeps forward into the anterior and medial part of the temporal lobe, separating the gray matter of the ventral claustrum into islands. It would appear that by way of these accessory uncinate fibers the cortex adjacent to the temporoinsular groove might have access into the deep gray matter of the amygdala and the ventral claustrum.

The ventral part of the claustrum is closely related to the amygdaloid nuclei, being contiguous with the lateral group, thus justifying the term claustroamygdaloid complex. It should be noted that in man the islands of the ventral claustrum

appear to extend forward into the anterior and medial part of the temporal lobe. This is well shown in Figure 14. There is no doubt that this claustral gray matter lies within the zone from which many of the stimulation responses were obtained. The functions and precise connections of the extensive area of gray matter making up the claustrum are unknown. It has rarely received mention in the many stimulation and ablation experiments carried out so intensively on the temporal lobe and limbic system.

The anterior commissure, which in primates is largely nonolfactory, fans out into this region, being most prominent in sections taken between 3 and 4 cm. from the temporal pole (Fig. 13). It affords an anatomical pathway for bilateral connections between inferior frontal, temporal, and insular cortical regions. Its anterior fibers run directly into the zone of the claustroamygdaloid complex.

The folded cell layers of the hippocampus begin at 4 cm. from the temporal pole and overlap the posterior part of the amygdaloid complex. The anterior end of the long bundle of fibers making up the cingulum also reaches into the claustroamygdaloid region at the tip of the temporal horn.

Wide connections of the cortex of the anterior temporal region have been defined by electrophysiological techniques by Marsan and Stoll (1951)[12] and, although the temporal opercular cortex, limen insulae, and claustroamygdaloid complex were not studied, their results in relation to the connections of the uncus have a bearing on the present study. Evoked responses were produced in the uncus by stimulation of the hypothalamus, thalamus (including the thalamic reticular system), and periaqueductal gray matter. After-discharges were recorded from the uncinate cortex after stimulation of the caudate nucleus, substantia nigra, and thalamus. Since Pribram, Lennox, and Dunsmore [13] described connections of the temporal polar cortex into the amygdaloid nucleus, it is possible that some of the responses involving the cortex of the temporal pole and uncus obtained by Marsan and Stoll [12] may be mediated by way of the amygdaloid nucleus.

Another pathway which should be considered from this region is the projection from the hippocampus by way of the fornix to the diencephalon and cingulate cortex, the regulatory function of which has been emphasized by recent physiological work.

The large fiber bundles—the uncinate fasciculus, the anterior commissure, the cingulum, and the external capsule—would appear to be capable of providing for anatomical connections between this periamygdaloid region and widespread regions of the brain.

Physiological Studies of the Periamygdaloid Region.—A number of observations from physiological studies of the amygdala and the uncinate and insular regions have a bearing on the present problem. Ferrier long ago noted movements of the lips, tongue, and cheek pouches from stimulation of this region in monkeys, and interpreted these as olfactory or gustatory reflexes. More recent work from different sources has shown that stimulation of the uncus in cats and monkeys produces autonomic responses, including changes in blood pressure, arrest of respiration, vocalization, and masticatory movements. Similar responses are obtained from the anterior cingulate gyrus and from the anterior insula. Kaada (1951)[14] found that from the anterior hippocampus, amygdala, and pyriform region, after-discharge could be obtained with intensities lower than those from other cortical regions. With stimulation of the amygdala by implanted electrodes in the unanesthetized

animal, he produced attacks of arrest of movement and of respiration, with licking, chewing, swallowing, micturition, pupillary dilation, turning of the head and eyes to the opposite side, and searching movements. Some of these features resemble those seen during attacks of automatism in patients (Table 2). Inhibition of spontaneous, reflex, and cortically induced movements was also produced by stimulation of the amygdaloid area, and Kaada suggested that these effects are mediated by the amygdaloid-stria terminalis connections to the hypothalamus and septal regions. Various types of suppression of the ECG, some being generalized, were also noted. Further interesting findings are those of Liberson, Scoville, and Dunsmore (1951),[15] who produced profound respiratory arrest, changes in consciousness, and amnesia from stimulation of the uncinate region in psychotic patients. They suggested that these effects were mediated by the amygdalohippocampal system.

Relation of the Amygdala to Diffuse Projection Systems.—From the present studies it is evident that automatism in man, whether induced by stimulation or occurring spontaneously, may be accompanied by initial suppression of electrical activity involving one or both temporal lobes or more generalized regions of the cortex. This observation may be taken as evidence that the local discharge in one periamygdaloid region fires into a subcortical mechanism which is related to both hemispheres. Such close relation of the amygdaloid region to the reticular systems was suggested by the findings of Marsan and Stoll, noted above. This work is now further substantiated by experimental studies (Feindel and Gloor, 1954)[16] in cats, in which stimulation of the claustroamygdaloid complex on one side can produce suppression followed by after-discharge not only in the corresponding region of the opposite side but also in the brain stem or ascending reticular formation. Such after-discharge is associated with chewing and licking and arrest of spontaneous movements. Moreover, stimulation of the amygdaloid region gives suppression of the electrical activity in local or general regions of the cortex, which is strikingly similar to the effect of stimulation of the brain stem reticular formation. Suppression of cortical spikes evoked by strychnine can also be effected by stimulation either of the amygdaloid or of the brain stem reticular system. This response resembles those obtained in patients and illustrated above by Cases 1 and 5.

These findings suggest that the amygdaloid gray matter can be considered as a diffuse projection system, similar to the brain stem reticular formation (Moruzzi and Magoun, 1949[17]) and the intralaminar system of the thalamus (Jasper, 1949[18]), in that it is capable of exerting diffuse regulatory effects on other cerebral regions. With such widespread effects on the cortex and with these pathways into deep diencephalic structures, the amygdaloid region might well provide an anatomical structure of great importance in the mechanisms of memory recording.

Localization of Discharge in Automatism.—The mass of experimental data on ablation studies of the temporal lobe by numerous workers has been presented in excellent reviews by MacLean,[19] Kaada,[14] Fulton,[20] and others, and need not be mentioned here in detail. The results on the whole give considerable experimental evidence to support the conception that this region of the limbic system, particularly the amygdaloid region, plays a role in the control of behavior and of autonomic changes considered to be emotional. It may be added from the evidence of

the present studies that this same region is also concerned in the processes of memory recording and the maintenance of normal conscious states, both of which are obviously essential factors in the mechanism of behavior.

Stimulation within this area has produced automatism in patients who were under local anesthesia at the time of operation. Stimulation of other regions of the cortex has not produced automatism in our experience, save for exceptional instances, which, for reasons explained above, may be discounted. In particular, it should be noted that stimulation of the temporal pole has not produced automatism, even when this is the site of active spiking, as indicated on the EEG and as seen on the electrocorticogram. Such anterior spike "foci" may therefore be interpreted as being projected from actively discharging temporal gray matter folded in the depth of the Sylvian fissure or lying still deeper, in the amygdaloid region, beneath the temporoinsular cortex. This deep region of gray matter about the amygdaloid area, overlaid by the large mass of temporal cortex, can be reached only by deep stimulation or by surgical exploration after removal of the temporal pole. Nevertheless, its implication in automatism is being confirmed by the more frequent production of automatism by stimulation in recent cases. However, the mechanism by which epileptic discharge in this zone produces automatism remains to be determined.

In many patients, the automatic behavior appears at the initial stages of the seizure. Indeed, if the features described by some patients as difficulty in thinking or remembering may be interpreted as an actual initiation of the automatic state, it can be said that their seizures may be called primary automatism. Examples of primary automatism, with no preceding aura, have been reproduced by stimulation of the periamygdaloid region. This would further indicate the early and specific involvement of this zone by epileptic discharge producing automatism.

Amnesia is always present during automatism, and there may be impairment of consciousness. The amnesia may even outlast the period of apparent confusion. It may be proposed, hypothetically, that epileptogenic discharge takes place during automatism in this area which forms a portion of the memory-recording mechanism of one temporal lobe. The discharge interferes with the central portion of this mechanism, thus interfering with memory recording. The interference is ictal and continues during a subsequent postictal period until the gray matter involved recovers from its fatigue.

It seems likely that discharge confined locally to the amygdaloid area does not produce amnesia. Those patients who show amnesia continue in this state after cessation of stimulation, suggesting spread of after-discharge to deeper subcortical structures.

In spite of the deep connections of this region, it seems evident that the local lesion causing the epileptic discharge lies within the periamygdaloid area itself. This is demonstrated by the objective pathological and electrographic abnormality within this area at operation, and by the repeated observation that the successful arrest of attacks characterized by automatism depends upon adequate surgical excision of abnormal tissue in this particular area. It may also be noted that it is consistent with the view that tentorial herniation at birth may be a cause of temporal lobe seizures later in life (Earle, Baldwin, and Penfield, 1953).[21] The amygdaloid region would be involved in such a herniation on two counts—first, by the direct

mechanical distortion and grooving by the sharp tentorial edge and, second, by temporary interference with its blood supply by the concomitant compression of the anterior choroidal artery on the edge of the tentorium.

SUMMARY AND CONCLUSIONS

In a series of 155 patients operated upon for the treatment of temporal lobe seizures, 121 (78%) had attacks characterized by behavior automatism. This would include unresponsiveness, confusion, masticatory movements, and inappropriate but often elaborate behavior, for which the patient is later amnesic.

From a detailed analysis of the seizure patterns of 50 patients with temporal lobe automatism, it is concluded that automatism may be preceded by no warning, or by one or more warning features. There is, therefore, true ictal, as well as postictal, automatism.

Among the variety of phenomena which may precede the automatism in the seizure pattern, the commonest are abdominal sensation, conscious confusion, tonic or adversive motor features, somatic sensation, cephalic sensation, and feelings of unreality.

Conscious confusion followed by tonic or adversive motor features constitutes a common epileptic "march" leading into automatism.

Stimulation of the brain in the conscious patient undergoing surgical treatment for temporal lobe seizures has produced automatism and amnesia, sometimes with widespread suppression of the electrical activity of the cortex. Twelve cases are presented to illustrate these stimulation responses.

The area responsible for the initiation of behavior automatism appears to center in the periamygdaloid region. This includes the uncus, the amygdaloid nucleus, the ventral claustrum, and the temporoinsular cortex deep in the anterior part of the Sylvian fissure. The anatomy of this complex region is reviewed.

It is pointed out that the periamygdaloid region is particularly susceptible to involvement by tentorial herniation, either by direct mechanical distortion of the tentorial edge or by interference with its blood supply by compression of the anterior choroidal artery. The present studies, therefore, are consistent with previous views that incisural sclerosis produced by tentorial herniation at birth is a cause of temporal lobe seizures coming on later in life.

Evidence is presented that the deep mesial structures of the temporal lobe are concerned in motor responses which may be additional to those derived from the Rolandic, supplementary motor, and second sensorimotor areas.

The term uncinate fits is inappropriate to describe attacks with olfactory and gustatory aura, since only about 5% of patients with behavior automatism have such features. It is noted that temporal lobe seizures with behavior automatism more closely correspond, as regards both the seizure pattern and the site of the pathological lesion, to the uncinate fits as described by Hughlings Jackson.

The present observations, together with subsequent animal experiments, would support the view that the claustroamygdaloid gray matter can be considered along with the diffuse projection systems of the thalamus and brain stem as a region capable of exerting diffuse regulatory effects on other parts of the brain. Evidence, in particular from the studies in man, indicates that the periamygdaloid region is

also concerned in the processes of memory recording and the maintenance of the normal conscious state, both of which are clearly essential factors in the mechanism of behavior.

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Special Article

CLASSIFICATION OF THE EPILEPSIES WITH PARTICULAR REFERENCE TO PSYCHOMOTOR SEIZURES

SIR CHARLES SYMONDS, K.B.E., C.B., D.M., F.R.C.P.
LONDON

IT IS NO easy task to attempt a classification of the epilepsies today, at a time when knowledge is being gained at such a pace that perspectives are continually changing; but if we are to make the best use of what is new, we need some kind of a filing system which is comprehensive and permits cross reference. The admirable papers written on the subject by Penfield,[1] Lennox,[2] and McNaughton [3] in recent years invite attention and provoke thought, for I doubt whether any neurologist will be entirely satisfied with anyone else's criteria. When, however, he sets out upon a classification of the epilepsies for himself, he becomes aware of many difficulties which were not at first apparent, and among these the usage of words is as great as any other. Once a word has obtained the authority of custom to cover an association of seizures with a particular anatomical landmark or EEG pattern, its value is lessened for purposes of clinical description. Despite the difficulties, it has seemed to me worth while to embark upon this task, if only with the aim of defining certain principles which I believe should guide classification whatever the nomenclature may be.

The general principles which I have in mind may be simply illustrated by the consideration of a peripheral nerve lesion. Let us suppose a case of injury by pressure of the musculospiral, or radial, nerve. First, we note the clinical symptoms, a flaccid paralysis of certain muscles in which the most conspicuous feature is inability to extend the outstretched wrist and fingers. We then proceed to the anatomical aspect of diagnosis and from examination of the muscles paralyzed determine the situation of the lesion. The physiological state of the nerve is then investigated by electrical means—let us suppose that the electrical reactions in the paralyzed muscles three weeks after the injury are normal. The pathology is established for us by the fact that the paralysis immediately followed pressure upon the arm while the patient was pinned down in an overturned car. Clinically speaking, this case is one of wrist drop; anatomically speaking, it is a lesion of the radial nerve above the elbow; physiologically speaking, it is neurapraxia, and pathologically speaking, it is a pressure paralysis. For the complete description of the case each of these terms is necessary, and each of them belongs to a different order of classification. Flaccid paralysis is one of a number of different motor affections of the upper limb, the others being spasm, tremor, and so on. The radial nerve is one of many peripheral nerves classified by the anatomist; neurapraxia belongs to another series of terms devised to cover failure of conduction of the nervous impulse of different types,

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and the pathologist again has his own list of causes, including trauma. This method of multiple classification may seem superfluous in such a simple case as we have been discussing, but unless it had been generally followed, the science of medicine could not have been developed, for it is by cross reference from one category to another that knowledge is gained. I submit that in the classification of the epilepsies we ought to follow the same plan, admitting the necessity for separate categories of data, clinical, anatomical, physiological, and pathological, and making use of separate terms within each category so that correlation may be achieved without confusion.

In the epilepsies we should first seek to define and name clinical patterns and arrange them for convenience in some kind of order, and proceed to do the same with the data of anatomy, physiology, and pathology. For practical purposes it will be useful to record the data in any particular case under the appropriate headings, so that they are set forth in four parallel vertical columns. The data in the anatomical column refer to the site of the discharging lesion; those in the physiological column are concerned with disorders of cerebral function proved or assumed to be associated with the seizure, while the pathological column will contain data related to the disease responsible for the liability to seizures, when this is known. It is, I think, of value to add a fifth column in which to record observations upon the effect in suppressing the seizures of a particular drug. The physiological column may conveniently be divided into two sections, one for electrical, the other for biochemical, data. The scheme will then be as follows:

Clinical	Anatomical	Physiological		Pathological	Therapeutic
		Electrical	Biochemical		

Under the clinical heading will be recorded for each case or group of cases the pattern or patterns of the seizures. In the anatomical column the known or presumed site of the discharging lesion will be stated. This may be determined by clinical deduction, the demonstration of a pathological lesion, or the situation of the discharge in the EEG. The site of the discharge may be circumscribed, for example, temporal, occipital, or Rolandic; it may be generalized throughout the cortex, or it may be central, the evidence for this being a bilateral synchronous 3-per-second spike-and-wave pattern of the EEG. This EEG pattern, when present, will be recorded in the column for electrical data as a specific accompaniment of certain seizures. Under the biochemical heading will fall disorders of cerebral function, proved or assumed to be associated with certain seizures—anoxia, hypoglycemia, and uremia, for example. The pathological data will be derived from the symptoms and signs and from special investigations, including the EEG, which may reveal a focal destructive lesion, a mass interposed between cortex and electrode, or the EEG pattern of inclusion encephalitis. In the therapeutic column will be recorded such terms as dione-responsive, primidone (Mysoline)-responsive, and so on.

The aim of such an arrangement will be, of course, to establish correlation of the data in the different columns, but it is an arrangement which provides opportunity for recording differences as well as similarities, the differences being equally as important.

The most significant correlation that will appear is that in which the clinical pattern is that of momentary seizures (loss of consciousness, falling attacks, or myoclonus)—the anatomical site is central; the electrical disorder is of the 3-per-second spike-and-wave pattern, and the pathological cause is unknown. This combination has been often enough observed to deserve a name, and the name it has been given is true petit mal. If, now, we make use of the fifth column, we shall find that some cases of true petit mal are dione-responsive, others are non-dione-responsive. Here the observation of a difference provides opportunity for further correlation. Are there, for example, differences in age incidence, frequency, or pattern of attacks between the dione-responsive and the non-dione-responsive group?

If, however, we take as our point of departure the column for physiological data, we shall find that in some cases presenting the 3-per-second spike-and-wave discharge, though the discharge is bilateral and synchronous and the anatomical site therefore is presumably central, the seizures, or some of the seizures, take the form of generalized convulsion with loss of consciousness. Such attacks are correctly included by McNaughton [8] under the category of central epilepsy, but they cannot, of course, be described as petit mal. If instead of the physiological column we take as our point of departure the clinical column, we shall, I think, have to admit that there are seizures clinically identical with those of true petit mal, but without the EEG pattern which has been accepted as essential for this diagnosis. This is certainly true of momentary attacks of loss of consciousness, which may be observed with discharge arising in various parts of the brain with corresponding EEG foci. Apart from these there are a great many seizures that cannot be classified as true petit mal, but which have in common with true petit mal the clinical feature of momentary duration. All seizures of this kind were formerly covered by the term petit mal, but petit mal has now been given another meaning and can no longer be used in its old sense without confusion. The distinction now sometimes made between petit mal and true petit mal is of no real help. It would seem, therefore, that a new term is needed to replace petit mal for momentary seizures. Momentary seizure might itself suffice, but, with regard to the use of other terms, perhaps minimal seizure would be better, provided that it is clearly understood that minimal refers only to seizure duration. The other terms to which I have referred are, of course, major and minor. Major seizure is a useful term for the description of attacks in which there is generalized convulsion with loss of consciousness, whether the generalized convulsion appears at the onset or is preceded by local spasm or other focal symptoms. The term minor epilepsy has been used much more loosely, often to include what was called petit mal. The objection to minor epilepsy—or, for that matter, to grand mal, or major epilepsy—is the implication that epilepsy is a disease. Minor seizure is for this reason a better term and could be used in a descriptive way to include all attacks which are not major or minimal seizures as already defined. Of course, the use of all these terms is simply a matter of convenience, but I believe that it may be of practical value. One of the advantages of the term minimal seizure

is that it would include true petit mal and at the same time provide for the classification in terms of anatomy, physiology, pathology, and therapeutic response of other minimal seizures.

Many seizures are of momentary duration, and the focus of discharge may be in various situations. There is plenty of clinical evidence for this, and the EEG sometimes indicates a focal point of discharge for momentary seizures whose local character is not clinically apparent. But there are also momentary, or minimal, seizures in which there is no evidence, from clinical pattern, EEG, or pathology, either of localized or central discharge. For the purpose of scientific classification the generic term minimal seizure provides for the recognition of different species of minimal seizures. It is possible, also, that the division of seizures into the three groups major, minor, and minimal may have practical value for observing the effect of certain drugs. It seems, for example, that the diones may be effective for minimal seizures other than those of true petit mal, and that primidone may be of particular value in controlling major seizures. Of course, the same patient may at different times have seizures of different degrees. This is true of focal epilepsy and of central epilepsy, as well as of the unlocalized varieties.

It will be noted that the classification here suggested provides for the inclusion of EEG data under several headings. The EEG of true petit mal stands alone in representing a specific physiological disorder associated with certain seizures. The EEG may also provide data determining the anatomical site of the lesion and its pathology.

So far no mention has been made of psychomotor epilepsy. I agree with McNaughton in believing that this term should be discarded, but for different reasons. He argues that "there is still insufficient basis for a sound classification of psycho-motor-seizures." I should rather agree with Lennox [2] that "the term psychomotor epilepsy might be supplanted by temporal epilepsy." As this question of terminology is important, I shall propose to discuss what has come to be called psychomotor epilepsy in its historical perspective.

In 1888 there appeared in *Brain* a paper by Hughlings Jackson entitled "On a Particular Variety of Epilepsy." [4] In this paper, based upon the notes of 50 cases, Jackson described in detail the clinical features of a group of attacks which had not up to that time been generally regarded as epileptic. In such attacks he observed there was as a rule neither generalized nor local convulsion. There was seldom loss of consciousness, always, as he thought, some defect of consciousness; but there was something more than this, and this something more was essentially a disorder of the psyche, manifest in a disturbance of thought, perception, feeling, or behavior.

In his description of these seizures Jackson paid particular attention to what he called the dreamy state, a state in which there is a vague recollection of something long forgotten, abrupt, transient, and recognized by the sufferer as abnormal. In order to convey to his readers the quality of these attacks, he quoted in several cases the patient's own words. One was a medical man, who described his first attack as follows:

"I was carelessly looking round me, watching people passing, when my attention was suddenly absorbed in my own mental state, of which I knew no more than that it seemed to me to be a vivid and unexpected recollection—of what I do not know."

There might, Jackson observed, be more positive recollection than this—the memory of a scene or conversation or the content of the dream might be imaginary, but seldom could the patient after the attack recall its whole content. Jackson, therefore, preferred the word reminiscence.

Taking the dreamy state as his point of departure, he went on to describe the symptoms he had observed to be associated with it in different seizures. These varied somewhat from case to case, and at this point in his argument Jackson says, referring to the title of his paper:

> I shall continue to use the expression "variety of epilepsy" for a group of different epilepsies, each of these agreeing in presenting the dreamy state. . . . Although I use the expression "variety of epilepsy" as if there were a clinical entity "epilepsy," with complications, peculiarities etc. warranting subdivisions of it, there can be no question that there are at least as many epilepsies as there are paroxysms beginning with different "warnings." What we call the warning, this being the first event from, or during, the onset of the local, sudden, rapid and excessive (or briefly, epileptic) discharge, is the clue to the seat of the "discharging lesion." There are at least as many differently seated "discharging lesions" as there are different warnings of the paroxysms.

The symptoms observed by Jackson to be frequently associated with the dreamy state were briefly as follows: crude sensations of smell or taste; elaborate hallucinations of sight or, occasionally, of hearing; an epigastric sensation; a feeling of dread; movements of the lips and jaws resembling those of chewing, tasting, or spitting; aimless movements of the limbs, coordinated, not convulsive, and, finally, "exceedingly complex and very purposive-seeming actions during continuing unconsciousness."

Jackson's paper was shortly followed by others on the same subject, adding to the clinical description and recording three cases in which this particular variety of epilepsy was proved at autopsy to be associated with organic disease—tumor or softening—in one or the other temporosphenoid lobe. Some years later Jackson (1899) [5] proposed the term "uncinate group of fits" for his particular variety of epilepsy, on the basis of further postmortem examinations. He later wrote of this proposal:

> This was on the hypothesis that the discharge lesions in this case are made up of some cells, not of the uncinate group alone, but of some cells of different parts of a region of which this gyrus is part—the uncinate region.

I do not think I need apologize for quoting Jackson at such length, for both in his clinical observations and in his deductions from them in terms of anatomy and physiology, what he wrote more than half a century ago is remarkably up to date. At the time, however, his views did not command general acceptance, and the term "uncinate group of fits" was little employed. Gowers [6] in the second edition of his famous monograph on epilepsy, makes no use of it. He mentions the dreamy state as being sometimes associated with a special sense aura and refers (inaccurately) to Jackson's concept in a footnote, thus:

> Dr. Jackson proposes for the attacks with symptoms of the perception of flavour the name "uncinate convulsions" but we are only justified in referring the process to this region when there is evidence of a definite olfactory sensation.

Backed by the authority of Gowers, the view prevailed that the single criterion for uncinate attacks was an olfactory aura.

Psychomotor epilepsy is a term introduced by Gibbs, Gibbs, and Lennox,[7] in 1938, based upon the observation of a newly discovered pattern in the EEG which was thought to be associated with a particular variety of epileptic seizure. They wrote of "seizures ordinarily classed as psychic variants or equivalents" and went on to say:

> In these attacks the patient, though he may perform apparently conscious acts, is not subject to command; he may exhibit involuntary tonic movements; he may display psychomotor disturbances of a surly and unpleasant sort, and on recovery he has complete amnesia for the attack.

Based as it was upon a demonstrable electrical record, the concept of psychomotor epilepsy in these terms gained popularity, and it was widely supposed that a new clinical type of epilepsy had been recognized and that it could be diagnosed by the EEG. In the light of knowledge gained, or perhaps regained, since that time, Lennox [2] has recently reviewed the concept of psychomotor epilepsy, and his account of the clinical symptoms to be included within what he calls the "psychomotor triad" adds little to what had been described by Hughlings Jackson in 1888. The triad, as Lennox describes it, comprises motor phenomena, including abnormal behavior; automatism with amnesia; subjective psychic seizures, including the dreamy state, hallucinations of sight, hearing, smell, or taste, and episodes of mild confusion. He concludes that in view of evidence obtained from various sources the term psychomotor epilepsy might be supplanted by temporal epilepsy. He leads us back, therefore, toward Jackson's concept of the "uncinate group of fits." Temporal lobe epilepsy is doubtless a better term than uncinate epilepsy, for it seems from Penfield's observations that some of the epilepsies included by Jackson in the uncinate group are evoked by stimulation of other parts of the temporal cortex. This but confirms Jackson's qualification that by the uncinate group of fits he meant that the discharge arose from cells not of the uncinate group alone, but of some cells of different parts of a region of which this gyrus is part. This same qualification should equally well apply to the hypothesis of temporal lobe epilepsy. Judging both from clinicoanatomical observation and from the effects of stimulation, it would appear that some of the phenomena which Lennox would include within temporal lobe epilepsy are due to discharge arising in, or spreading to, the structures adjacent to the temporal lobe. For example, Penfield and Rasmussen [8] have obtained masticatory movements from stimulation of the cortex just above the island of Reil and epigastric sensation from the surface of the island of Reil, neither being obtained from stimulation of the temporal cortex itself. Automatic behavior in or after a seizure is not necessarily associated with temporal lobe discharge. It may occur with discharging lesions in the posteroinferior part of the frontal lobe also, and probably elsewhere. The temporal lobe is, of course, to be regarded not as a functional unit, but as a convenience of the anatomist for his purpose of classification. It would be absurd to suppose that the neurophysiological dispositions or circuits serving a particular function must be confined within the limits of a lobe. It would also be wrong to suppose that because circumscribed disease or electrical stimulation of the temporal lobe causes an elaborate visual hallucination, the hallucination is the expression of temporal lobe activity. The activity responsible for the hallucination may well be elsewhere, and probably involves wide areas. All we are really entitled to conclude is that discharging lesions in the temporal lobe can set this activity going. Having regard to these qualifications, which were well understood by Jackson,

we may accept the concept of temporal lobe epilepsy as a working hypothesis, and it is to be hoped that it will supplant the term psychomotor epilepsy, for which there was never much to be said, for the EEG pattern which gave rise to it has proved nonspecific after all. The EEG, however, has in other ways contributed greatly to our knowledge of temporal lobe epilepsy by demonstrating the discharging lesion in the form of localized repetitive spike foci. Correlation of spike focus with clinical pattern has thus not only confirmed what was already known about temporal lobe seizures, but has made possible the recognition as such of paroxysmal disorders of mood and behavior of a kind which had been suspected of being epileptic without proof. Jackson observed the feeling of dread in temporal lobe seizures. There may also be depression, excitement, and rage associated with corresponding behavior. The EEG, therefore, may reveal the epileptic nature of a symptom, but it is not a symptom. A temporal lobe spike focus is one thing; an epileptic seizure is another. The two phenomena may be associated, but they belong to different orders and need separate terms for their classification.

SUMMARY

To sum up, temporal lobe epilepsy comprises a group of epilepsies having in common a site of discharge in the region of the temporal lobe. The clinical pattern of these seizures varies with the precise situation and direction of spread of the discharge. The seizures may be of major, minor, or minimal degree. We may hope that with better correlation of clinical pattern with demonstrable lesion or EEG focus more accurate localization will be achieved. The clinical features of anterior and posterior, deep or superficial, discharging lesions may prove to be distinct. The pathological classification of the temporal lobe epilepsies is a separate problem. Why are focal seizures in this situation so common without any clinical evidence of coarse or progressive lesion? The concept of incisural sclerosis from birth injury (Earle and associates [9]) may provide an answer, but there is much scope still for the neuropathologist in the elucidation of this problem.

87, Harley St., W.1.

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Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Walter Wegner, M.D., President, Presiding
Regular Meeting, March 18, 1954

Hypertensive Hemorrhages of the Pons and Cerebellum. Dr. Harry C. H. Fang and Dr. Joseph M. Foley.

Subtentorial brain hemorrhages, pontine or cerebellar, not infrequently present considerable difficulties in clinical diagnosis. Of 286 hypertensive hemorrhages at Boston City Hospital in 10,000 consecutive autopsies, 231 (80%) were cerebral, 29 (10.1%) were cerebellar, and 26 (9.1%) were pontine in location. Hence, nearly one out of every five cases in this series of primary brain hemorrhages involved either the pons or the cerebellum.

At the end of the first 10 hours after onset of symptoms nearly 70% of the pontine cases were dead, whereas only 40% of the cerebral and 26% of the cerebellum group succumbed to the apoplectic assault.

Two cases studied from both the pontine and the cerebellar series (complete with anatomic confirmation) were presented to emphasize difficulties in clinical diagnosis of such cases. The "classic features" that make it possible to recognize either pontine or cerebellar apoplexy are seldom encountered in an extensive volume of clinical material.

DISCUSSION

Dr. Raymond D. Adams: Vascular disease represents the most frequent type of neurological disease we have to deal with.

Have you been able to reach a solution to any of the basic problems concerning hypertensive brain hemorrhage? There is a controversy as to what causes these hemorrhages—the hypertension itself or some damage to the vessel wall. The common teaching is that hemorrhage can occur from either cause. The arteries of the human brain can stand pressure many times greater than that from hypertension. Some kind of vascular disease must, therefore, exist. Dr. Zimmerman thought it was atherosclerosis. Has that been your finding?

Dr. Paul I. Yakovlev: Did you see any hyperthermia in the patients who survived more than a few hours?

Dr. Leo Alexander: Two cases come to mind. One patient, from the Boston City Hospital, had had an episode about three years before her second, fatal one. Autopsy revealed side by side an old cyst and a fresh pontine hemorrhage. This patient, a bank clerk, had collapsed, vomited, and developed a left hemiplegia, with some eye muscle disturbances and nystagmus, three years before; she recovered, and the diagnosis of multiple sclerosis was made. She remained well for about three years, when she had another, similar episode. She died from the second, much larger hemorrhage.

The other case is one I saw with Dr. James L. Poppen. There was sudden onset of left (upper and lower) facial paralysis; nystagmus, vertical and to the left, and left hemiplegia with bilateral spastic signs. The diagnosis of thrombosis of the basilar artery was made, and confirmed by Dr. Poppen, proving the occlusion of the basilar artery shown by vertebral arteriograms. This woman recovered and is now symptom-free. This case supports the authors' thesis that some of these patients do survive.

Dr. John N. Walton: In this paper by Drs. Fang and Foley the relatively high incidence of pontine and cerebellar hemorrhages was very striking. I had always had the impression that primary cerebellar hemorrhage was less common than intrapontine bleeding, although I have been impressed by the frequency with which patients suffering from blood dyscrasias, such as aplastic anemia, have bleeding into the cerebellum.

Like Dr. Adams, I have often wondered about the etiology of primary brain hemorrhage. Bleeding always seems to occur deep within brain substance, from terminal branches of the arteries of supply. It seems that atherosclerosis cannot be the whole story, since large arteries severely affected by atheroma so rarely rupture. The exact responsibility of hypertension is also very difficult to evaluate.

This paper also contains information of value to neurosurgeons. Now that a small proportion of cases of primary intracerebral hemorrhage are being attacked surgically in order to remove blood clot, it will be important to remember that in a significant proportion of such patients bleeding may be primary within the cerebellum or the pons and the clinical pictures produced may sometimes be very similar.

DR. HARRY C. H. FANG: Dr. Adams asked whether or not we have any data about the pathogenetic background of such cases. Our present scope has been restricted to the analysis of the clinical data and emphasis on the survival period. We have always wondered about the nature of the pathogenetic process underlying such hemorrhage states also.

As regards Dr. Yakovlev's question about hyperthermia in our pontine group, we have not presented our analysis of the clinical data here. However, hyperthermia featured significantly in at least 4 of 19 cases. In one of them the temperature reached 109 F. before death.

Critical Ages for Parental Death in Psychoneurosis. DR. HERBERT BARRY.

There is a sex difference in the frequency of bereavement in cases of psychoneurosis. If the ages of all persons at the time when their parents die are charted, there are more parental deaths as the child grows older. In psychoneuroses, three distinct types of curves appear. (*a*) When the patient and the parent are of opposite sexes, there is a progressive increase in the number of parents who die, as in normal persons. (*b*) In female psychoneurotics, maternal deaths reach a peak during infancy. (*c*) In male psychoneurotics, deaths of fathers appear to reach a maximum during adolescence.

The second finding is most striking. The number of female psychoneurotics whose mothers died before they were 3 years old is four times the expected figure. This increase is highly reliable. It is confirmed by data on divorce; after parental separation more female psychoneurotics were prematurely deprived of their mothers' care.

Previously, emphasis on "broken homes" has obscured the importance of parental deaths and the significance of critical ages for bereavement. Nevertheless, several investigators have reported slightly higher parental death rates for neurotics than for controls. Bereavement is commoner in female than in male delinquents. These findings are consistent with results of the present study.

An Antiepinephrine Factor in Treatment-Resistant Schizophrenia and in Intractable Psychalgia. DR. LEO ALEXANDER.

Among the abnormalities of autonomic reactivity revealed by the epinephrine-methacholine (Adrenalin-Mecholyl) test (Funkenstein test) inadequate response to epinephrine, defined as a blood pressure rise of less than 20 mm. Hg upon intravenous injection of 0.025 mg., characterized the group with the lowest recovery potential and responsiveness to treatment. Prior to the present study I had found that patients showing such reduced response to epinephrine did not respond to any treatment except insulin coma.

The present study is an attempt to investigate the physiological characteristics of reduced response to epinephrine. It was found that either atropinization or administration of cortisone or corticotropin (ACTH) counteracted the inadequacy of response to epinephrine, suggesting that this inadequacy of response is probably caused and maintained by an antiepinephrine factor of cholinergic, muscarinic nature, which can be counteracted by atropine, as well as by the production of a hyperadrenal state. Two patients in whom the response to epinephrine became normal on corticotropin therapy showed marked clinical improvement. Two other patients improved clinically after maintenance of atropinization for several weeks. These preliminary experiences warrant more extensive therapeutic trial of corticotropin, as well as of atropinization, in patients exhibiting this type of autonomic reaction pattern.

DISCUSSION

DR. RAYMOND D. ADAMS: I should like to know how many normal persons have been tested in this way, and what are the individual variations in response to epinephrine. A failure to respond to a drug may have different meanings. Could it be an individual variation that we do not understand?

DR. DAN H. FUNKENSTEIN: Dr. Alexander makes two points in his paper: The first is that when there is a small rise in blood pressure after the injection of epinephrine, atropinization of the patient will result in an increased rise in blood pressure after epinephrine, thus bringing the height of the elevation into the "normal" range. This finding he interprets as indicating the presence of an antiepinephrine factor. With this interpretation of the data I disagree. The reason that intravenous epinephrine raises blood pressure is that it increases cardiac output. Thus, in these cases epinephrine gave only a minimal increase in cardiac output. The most likely explanation of this phenomenon is that the cardiovascular reflex which prevents the rise in blood pressure from becoming too high is hyperactive. This reflex is most frequently mediated by the vagus. I believe that Dr. Alexander has shown us that such cases probably have increased vagal tonus but has given us no evidence that an antiepinephrine factor is present. Many investigators have searched for such a factor, but it has not as yet been found.

The second point made by Dr. Alexander is that either corticotropin or atropine in these patients changes the reaction to epinephrine and that they will then respond to treatment, although previously they would not. I am very chary of any new treatment in psychiatry and must cite Arthur Ruggles to the effect that no new treatment in psychiatry should be accepted until 10 years have passed, owing to the many uncontrollable factors at work in psychiatric patients. Certainly, here the cases are too few to allow one to draw any conclusions as to whether or not this method has therapeutic possibilities. This is not to discourage experimentation with new therapeutics but to urge caution, with several years of work and careful controls before presenting them.

DR. LEO ALEXANDER: I agree with Dr. Adams when he says that this inadequate response to epinephrine is an individual trait, the nature of which is obscure. However, it is a trait which is significantly correlated with greatly reduced capacity to recover from mental disease and to respond to treatment.

A statistical study of 200 consecutive mental patients in private practice, which I completed recently, revealed that markedly reduced response to epinephrine, such as is characteristic of Funkenstein's original Group V, constitutes the most unfavorable prognostic group of all. The differences among all reaction groups of my 200 patients were found to be statistically significant at the 0.03 level. Inspection of the data made possible by a $2 \times k$ chi-square analysis revealed that Group V was the greatest contributor to this difference as the most unfavorable group. In my largely acute clinical material, comprising this first series of 200 patients, Group V was represented by 10 cases, that is, by 5%. Six additional patients were encountered among an additional 50 patients seen in the past one-half year, since the completion of the above survey. The physiologic studies reported in this paper were carried out on these six patients.

In a recent pilot study which I undertook on a chronic ward of the Boston State Hospital, I found that among 10 consecutive cases studied, 4 showed inadequate response to epinephrine. This finding, if confirmed by further studies, suggests that Funkenstein's Group V contributes significantly to the residue of chronic "incurable" patients that accumulate in the back wards of state hospitals. I have never seen inadequate response to epinephrine in normals not under stress. The fact that inadequate response to epinephrine, found in patients prior to treatment, is associated with low recovery potential and poor response to treatment is also illustrated in the case of a patient who, during her first psychotic episode in 1950, had shown adequate response to epinephrine and responded to treatment. When she relapsed three years later, her response to epinephrine had become inadequate, and this time she had also become unresponsive to all treatments except corticotropin.

The only exception to the implication of poor prognosis is the rare temporary occurrence of inadequate response to epinephrine during the inert, inhibited state following an intensive course of electroshock therapy, the response becoming adequate again when the patient proceeds to full recovery.

Most patients show an enhanced response to intravenous injection of epinephrine after electroshock therapy. The cause of this exceptional reduction of response to epinephrine after an intensive electroshock series is obscure.

In speaking of an antiepinephrine factor as responsible for this phenomenon of reduced response to epinephrine, I meant to apply this word in its widest possible sense. It could, of course, be a reduced tissue reactivity, as Dr. Adams surmises, or enhanced vagal tone, such as Dr. Funkenstein suggests. I am fully aware that I have no evidence whether the antiepinephrine factor is chemical or neural or, as is more likely, both, since vagus action certainly is inseparable from the vagus substance.

I am fully satisfied with the validity of my finding that patients showing inadequate response to epinephrine prior to treatment will show normal response to epinephrine if atropinized for a week or while treated with corticotropin or cortisone. I fully agree that the marked clinical improvement shown by four patients, temporary in one, is certainly insufficient to draw conclusions as to the usefulness of atropinization or of corticotropin or cortisone therapy in patients belonging to Funkenstein's Group V. However, I felt that the clinical observations made were sufficiently provocative to warrant communication, mainly for the purpose of discussion and, perhaps, stimulation of others to investigate the phenomenon which I described. I might say in this connection that as long ago as 1932 Leonhardt reported on the favorable therapeutic effect of atropinization in certain psychotic states. His treatment, although introduced 22 years ago, has never been adequately tested and, therefore, had no chance to stand the trial of time, because it soon became overshadowed by more generally applicable physical forms of treatment, such as insulin and electroshock, introduced soon thereafter. However, since the treatment of mental disease must strive toward ever-increasing specificity of indications, it certainly would be of interest to see whether Funkenstein's Group V perhaps constitutes the group to which this treatment may become applicable.

Walter Wegner, M.D., *President, Presiding*

Regular Meeting, April 15, 1954

Disorders of Character: Persistent Enuresis, Juvenile Delinquency, and Psychopathic Personality. DR. JOSEPH J. MICHAELS.

The suggestion that there is a specific class of psychopathic personalities of a persistent enuretic-delinquent type might lead to a reevaluation of the respective roles of constitution, maturation, and experimental development. The elaboration of the persistent enuretic pattern, characterized by a lack of control, should lead to a more intensive study of this type of malintegration and probably also of the obverse situation, in which very early control of the urinary sphincter establishes an "over-control" pattern, leading to a compulsive neurotic formation of character, where social adjustment is "too moral." Thus, at one extreme, impulsiveness would coexist with psychopathic personality (weak ego-persistent lack of sphincter control), and, at the other extreme, compulsiveness would go hand in hand with the compulsive neurotic character (strong ego-early sphincter control).

To make a place for persistent enuresis, juvenile delinquency, and psychopathic personality in psychoanalytic theory, it will be necessary to assess properly the urethral zone and to fit it into the ego-libidinal series of development, where disorders of character have rarely been allocated a specific locus. If to Freud's typology of erotic, compulsive, and narcissistic types the impulsive type of character (impulsive psychopathic and impulsive neurotic) can be added, a more comprehensive framework becomes available. Impulsiveness as related to the urethral zone would form the counterpart to compulsiveness associated with the anal zone. It might be that the traumatic neurosis and epilepsy could be more easily related to the impulsive type. The psychobiologic contrasts of the psychopathic personality and the compulsive neurosis suggest important social implications.

DISCUSSION

DR. G. COLKET CANER: Is it your feeling that because sufficient effort is not made to bring about effective sphincter training, children later become delinquent, or do you mean that the fact that efforts at sphincter training are not successful indicates that efforts to train children in other ways will also be unsuccessful?

DR. D. DENNY-BROWN: Has Dr. Michaels carried out cystometrography in any of these patients? Would he further define "persistent enuresis"? The common enuresis in childhood is a periodic, nocturnal enuresis, related to other evidence of the "nervous child"—night terrors, multiple tics, poor posture, etc. In such children cystometry does not demonstrate any defect in bladder mechanism. Such enuresis is a disorder of sleep. There is another type of enuresis, a more constant and persistent enuresis, that is diurnal as well as nocturnal, and not necessarily associated with any neurological or psychiatric disorder. One case, for example, was a professional colleague, a successful surgeon, who since earliest childhood had had such enuresis. He occasionally had diurnal enuresis, through inconvenience of facilities or through some excitement or exertion. On examination such patients are found to have complete inability to restrain sphincter control after the bladder is distended beyond 150 to 180 cc. Control was normal below that volume. We believe this type of enuresis results from an inborn, fixed difficulty in inhibiting the bladder beyond a certain volume of contents. There is no evidence of associated spina bifida, and the reflexes are quite natural. There is no other evidence of failure to develop corticospinal control. This type of persistent enuresis is indistinguishable from that seen early in some forms of diffuse brain disease, though it is then associated with some generalized increase in tendon reflexes. Is this the type of enuresis associated with psychopathic personality?

DR. WILFRED BLOOMBERG: There are two points I should like to make—the first, that we are well accustomed to the fact that the Kraepelinian and Bleulerian approach to the psychoses has given way to a more dynamic method of looking at things. What has lagged behind in this method of approach is the group called the psychopathic personalities. It is, therefore, of interest to me that whether Dr. Michaels is right or wrong in his formulation, he is at least prepared to present and define a category of psychopathic personality based upon a dynamic formulation that goes beyond our ordinary classification of character disorders.

Second, it is of interest that Dr. Michaels, a psychoanalyst, in looking at this problem, brings to us a combination of the psychoanalytic, the psychological, and the biological, in an over-all approach. He postulates constitutional factors as a possibility; he postulates that the same dynamic factors which lead to persistent enuresis are those factors which lead to psychopathic behavior in later life. I should assume that he takes it for granted that the psychopathic behavior is not due to the fact that the child was not toilet-trained in childhood, but that he was unable to respond normally to ordinary training because of other constitutional and dynamic factors. Dr. Michaels gives evidence that he thinks of a biological and psychological continuum.

These two aspects seem to me more important than the statistics which he has presented.

DR. JOSEPH J. MICHAELS: I am greatly indebted to Dr. Bloomberg for his remarks, in which he so well expressed the philosophy of my work. It is difficult to present succinctly 20 years of research within the confines of 20 minutes. I have tried to indicate how the data, which were first collected in 1933, have been reinterpreted with the changing in my frames of reference, beginning with neurology, psychiatry, psychobiology, and finally, psychoanalysis. Dr. Bloomberg emphasized that the work should not be looked on merely from a statistical standpoint, but should be viewed as an attempt to confirm a clinical hunch and a holistic way of looking at the personality. The question can be raised as to the validity of the thesis which I present—that persistent enuresis is a reflection of sphincter "immoraiity" and is a paradigm of the later social "immorality" of the person who has become a delinquent and a psychopath. It would seem to me that the congruence of findings from various samples of delinquents in this country by different authors in this country, in England, and in France would confirm the validity of the data.

Dr. Bloomberg's comment that there is an attempt at dynamic formulation which includes psychopathic personality is significant. The reason that the problem of the psychopathic personality has been so neglected in psychoanalytic thinking is the fact that so few patients with severe psychopathic disorders lend themselves to classic psychoanalysis. They have the least amount of suffering, conflict, reactive formations, and insight. The fact that in Freud's work there is little mention of psychopathic personalities is probably due to the fact that he himself probably treated few, if any, psychopaths. It is well known that before a psychopathic person can be successfully treated, he has to become a neurotic, in other words, make himself amenable to psychoanalytic treatment. Whether the hypotheses as presented are right or wrong, time will tell. However, I do not believe there is any doubt as to the statistical validity of the data.

I was not clear about Dr. Caner's question.

DR. G. COLKET CANER: Did you mean to imply that because children were not getting adequate sphincter training, they would become delinquents?

DR. JOSEPH J. MICHAELS: I am glad that Dr. Caner raised this question because it is not the implication which I meant to leave. However, the reverse is true in the sense that the histories of patients with severe delinquencies and severe psychopathies show a high frequency of persistent enuresis. If a child has persistent enuresis from birth, it does not mean that he will become a delinquent. However, I believe that if he does not become a delinquent, he will develop some disorder of personality of a rather serious nature.

In reference to the comments of Dr. Denny-Brown, unfortunately, we did not carry out intensive individual studies in the various samples presented.

In regard to cystometrography, we, ourselves, did not carry out such a study. However, I should like to quote from a study of H. Stalker and D. Band (Persistent Enuresis: Psychosomatic Study, *J. Ment. Sc.* **92**:324 [April] 1946).

"Eleven of 15 cases who were subjects of cystometrographic studies showed typical uninhibited neurogenic bladders with high pressure, low capacity, early uninhibited contractions and early desire to void, . . . the same type as is found in subtotal organic disease of the higher cerebral centers or spinal cord pathways."

As a definition, we considered that enuresis persisting beyond the period of 3 years would be considered unusual, that the bed-wetting would have to occur at least once a week. If the enuresis was diurnal, it was included in our original study on normals. We learned that it was important to make a distinction between persistent enuresis which is continuous from birth and enuresis which occurs after control has been established, a form which we have designated as neurotic enuresis.

Of great theoretical interest is the problem of why the sphincter control which is the last to be established in the development of children is the urinary one. When there is a loss of consciousness or in sleep, the sphincter control that is first lost is the urinary one. To date, I have been unsuccessful in learning why this is so.

Amorphosynthesis from Left Parietal Lesion. DR. D. DENNY-BROWN and DR. BETTY Q. BANKER.

A right-handed patient, aged 36, suffering from a left anterior parietal lesion, probably a small hemorrhage from a vascular anomaly, presented anosognosia, denial of right limbs, and disorder of dressing and shaving on the right side. There was loss of position sense and two-point discrimination in the right limbs, severer in the arm than in the leg, with loss of tactile localization in the distal parts of the limbs. The case has since been reported (A. M. A. ARCH. NEUROL. & PSYCHIAT. **71**:302-313 [March] 1954).

In this case the disorders of recognition usually found in patients with right parietal lobe lesion were present as a result of lesion of the dominant hemisphere. These disturbances are one-sided and are related to an elementary physiological disorder of the perceptual process called amorphosynthesis. They are not due to the bilateral disorders of conceptual function that constitute the true agnosias. Anosognosia was found to be related to defective morphosynthesis of somatic sensation, and not, as has been thought by others, to disturbance of visuospatial aspects of perception. There is release of a type of motor behavior called the "avoiding reaction," seen as an involuntary extension of the hand, and a disinclination to discuss the affected parts.

DISCUSSION

DR. ANDRAS ANGYAL: The authors localize the lesion responsible for amorphosynthesis in the parietal lobe. Previous reports have referred similar syndromes more specifically to lesions in the tissue along the interparietal sulcus, in the gyrus angularis, and in the gyrus supramarginalis. Is there in the authors' findings any evidence of such narrower localization?

I became interested in this type of phenomena, first, in connection with certain studies I made on space orientation, then, later, in studying a certain type of schizophrenia. The subjective symptoms of these schizophrenics showed striking similarities to patients with the so-called "interparietal syndrome." Objective neurological findings were, however, few (e. g., occasional defects of tactile localization, two-point discrimination) or entirely absent. The pneumoencephalographic findings in a small series of such cases were somewhat suggestive, but by no means conclusive, of cortical atrophy including the parietal area. On the basis of my own studies I

believe that in these types of symptomatology the psychologically central disturbance is in the organization of kinesthetic space, while other symptoms—e. g., deviations of visual perception—are secondary to this central disturbance.

DR. ROBERT S. SCHWAB: Were temperature and pain discrimination tested quantitatively in the two hands? Could the involved hand distinguish the same degree of light pain and temperature as that in the good hand, particularly in the early parts of this illness?

DR. RAYMOND D. ADAMS: This type of case throws light on several rather abstruse problems. I would agree that it is a striking example of what we call anosognosia in a right-handed person. There are few such cases on record. The difference between sensation and perception or, when there is a deficiency, between anesthesia and agnosia was emphasized. The traditional view is that sensation is the most elementary form of sensory experience, awareness of objects, and perception is the recognition and percept of objects. This view comes from structural psychology and the use of simple tests. The authors have shown that there is reason to doubt that sensation remains intact in many cases called agnosia. The important point is made by Dr. Denny-Brown, namely, that there may be a defect in sensation, provided one examines all the attributes of the stimulus itself—duration, time, and spatial relationships. This work supports the point that Goldstein and Bay have been trying to make, that agnosia is related to an elementary disorder of sensation. I am sure there is more to it than that. I should like to hear a further discussion from Dr. Banker or Dr. Denny-Brown. In a disorder as complex as agnosia, can one specify other deficiencies in the patient? The patient usually makes quite erroneous judgments of himself. He does not seem to appreciate a sensory defect and does not realize that something is the matter, or he ignores the part. Is there always some degree of confusion or inattentiveness? It seemed the anosognosia dropped out early. Did it clear up as the patient became more alert and more capable of focusing attention?

DR. DENNY-BROWN: In this case we have approached the problem as a study in phenomenology and do not have precise anatomical verification. We have one case with a good history of these disorders, but not studied in detail by ourselves, in which the lesion involved only the interparietal region on the lateral surface of the brain. Cases described by other investigators presenting these phenomena have had more gross lesions of the parietal lobe.

In the case reported here we did not carry out quantitative temperature tests. We were interested in the general nature of the disorder, particularly the heavy predominance of somatic spatial disturbance. Disorders of dressing and denial of limbs have previously been supposed to involve the visual spatial mechanism. This patient did show quantitative disturbance in relation to pinprick. It required two or three pins pricking the affected limb to abolish extinction by one pin on the normal side. It is interesting that the patient then says that it still feels like only one pin, but is clearer than the prick produced by one pin. Temperature and pain are disturbed in this way by cortical lesions, as are other sensations.

Dr. Adams points to a real difficulty in terminology. We must apologize for the word amorphosynthesis. It was difficult to find a new word for an intermediary stage of perception, distinguished from lower levels of sensory process, on the one hand, and from the more complex disorders called agnosia, on the other. Both amorphosynthesis and agnosia are disorders of perception. This patient was not confused in the ordinary sense at the time he denied his limbs, but confusion commonly complicates the picture in left hemisphere lesions. Disorientation of person commonly submerges anosognosia and denial of limbs. The abnormal behavior of amorphosynthesis is then overtaken by a larger process, which we would call disorientation of person, and the disorientation of speech that Head called syntactical aphasia. Confusion is usually shown by disorientation in time, place, or person. These disturbances are wide, all-embracing mental and symbolic concepts. In the patient we have discussed confusion in this sense was not present at any time, but behavior relating to a more elementary and restricted process (morphosynthesis) was confused. It is of special interest that the patient referred sensation in the fingers to the region of wrist and forearm, and sensation from the shoulder toward the forearm. There was a shift of perception toward the elbow. In his mind his limb was foreshortened. The limb has also become insignificant in a biologic sense, and is ignored by the organism. We believe that anosognosia belongs to this disturbance of behavior and is a derivative of the altered spatial quality of somatic sensations. It is certainly of interest that the disturbance of biologic behavior called schizophrenia should sometimes exhibit similar types of defect.

Variants of the Hysterical Pattern. Dr. Andras Angyal.

This report is a discussion of three variants of hysteria—simple hysteria, hysteria with negativistic defense, and borderline hysteria.

1. The basic pattern in hysteria is an adjustment by vicarious living. This pattern implies, on the one hand, an almost global repression of one's personality characteristics and, on the other, the acquiring of a substitute personality which may be internalized or remain external to the patient.

2. In hysteria with negativistic defense, there is an additional defensive layer around the simple hysterical structure. The defense is against one's own suggestibility and against the tendency toward excessive repression.

3. The borderline hysteric abandons himself to his pathological productions and deliberately cultivates them. He lives in a semidelusional phantasy world and has some tendency to act out his phantasies. In spite of the pathological inner life, these people may be efficient and superficially well adjusted.

DISCUSSION

Dr. Wilfred Bloomberg: I wonder whether Dr. Angyal could tell us in this formulation of his where hysteria leaves off and paranoia begins; where the pathological life begins, where hysteria leaves off and psychopathic personality with impulsive behavior begins. This means, of course, that I think there is a certain semantic confusion among us. We should need to start at the beginning and define our personal concepts of hysteria and hysterical personality. I admit this expresses a lack of understanding on my part, but I find the frame of reference somewhat strong and realize that it is unfair to expect Dr. Angyal to clarify it in a short time.

Dr. Joseph J. Michaels: One may well agree with Dr. Angyal's clinical description, in which he clearly showed a developmental sequence from the least disturbed to the less disturbed, and, finally, to a malignant type. When one deals with a psychiatric disorder, one observes that conflicts occur from all levels of the personality. Dr. Angyal demonstrates that although the predominant character structure of the patient may be hysteria, there may be an intense depressive factor. Such features as needing support and supplies from the outside world, a close relationship to a mother figure (symbiosis), the need for being liked, and the desire to eat a great deal occur frequently. It is of some interest that Judd Marmor emphasizes this depressive quality in hysteria in a recent paper (Orality in the Hysterical Personality, *J. Am. Psychoanalyt. A.* **1**:656 [Oct.] 1953).

The second type, which Dr. Angyal describes as hysteria with negativistic features, may also be regarded as having a paranoid admixture. Finally, the third type—the malignant form of hysteria—borderline in nature and giving an impression of a schizophrenic coloring, indicates regressive components from the deepest levels of the personality.

Thus, each person has his own specific major character structure, with conflicts and unique defense mechanisms emanating from all levels of the personality. From my clinical experience, I have often had the impression that there is a "psychotic hysteria character," and I think this tallies with Dr. Angyal's excellent description of the malignant type of hysteria.

Although Dr. Angyal may have a different theoretical frame of reference than Dr. Bloomberg and myself, nevertheless, I can agree with his keen clinical descriptions, which he presents so vividly in an ascending degree of severity.

Dr. Andras Angyal: The nosological consideration was not my primary interest. Rather, I wished to describe a specific type of neurotic pattern, the method of "vicarious living," and certain layers of defenses which may be superimposed on it.

Depressive features do occur in these clinical pictures, but by no means are they constant or striking.

Dr. Bloomberg's remarks seem to refer mostly to what I called borderline hysteria. Indeed, for some time I myself was uncertain as to the nature of this condition, trying, e. g., to understand it as some atypical paranoid state, but extensive study of a series of such cases convinced me of its basically hysterical structure. The phantasy productions of these patients are clearly different from the delusions of psychotics. These patients differ in several respects, also, from psychopathic personalities, particularly by the tremendous amount of anxiety which they exhibit.

CHICAGO NEUROLOGICAL SOCIETY

Douglas N. Buchanan, M.D., *President*

Meyer Brown, M.D., *Secretary*

Regular Meeting, May 11, 1954

Surgical Treatment of Syringomyelia. Dr. Loyal Davis and Dr. Nicholas Wetzel (by invitation).

In this paper, illustrated by lantern slides, the essayists discussed the technique of and the results in the surgical treatment of syringomyelia.

DISCUSSION

Dr. Richard Richter: An appreciable number of these patients had x-ray treatment before operation. Was it your impression that they obtained any benefit from x-ray treatment before surgery was performed?

Dr. Alex J. Arieff: Was the indication for surgery just syringomyelia, or was there an indication that there might have been a spinal fluid block or sudden change in the clinical picture? I can recall one of these patients seen at the Northwestern University Clinic over a period of years; he was greatly disabled but was still ambulatory. He was operated on for a block. At operation a thin shell of spinal cord was left. In spite of this, after operation he could walk very much better. He lived for some years after and was sent to Oak Forest. From the description of the thin spinal cord he should have had no function at all.

Dr. Nicholas Wetzel: So far as x-ray treatment was concerned, most of these patients, strangely enough, had their x-ray treatments at the University of Chicago. The only one we treated with x-ray was the one shown in the movie. He was postoperatively given x-rays in the doses mentioned because someone attributed to Dr. Davis the remark that he thought the x-ray therapy was beneficial. I later found that Dr. Davis did not think it had much effect. It did not seem to have much effect in altering the course of the disease.

The diagnosis of syringomyelia was not made until surgery. In a number of these cases it was a question whether they had a spinal cord tumor or some other surgical type of lesion. None of the patients had myelomas or any of the other cysts.

Rare Defects of Congenital Origin in the Nervous System: Presidential Address. Dr. Douglas N. Buchanan.

Election of Officers for 1954-1955.

President	Secretary-treasurer
Benjamin Boshes, M.D.	Oscar Sugar, M.D.
Vice-president	Councilor
John J. Madden, M.D.	Douglas N. Buchanan, M.D.

ILLINOIS PSYCHIATRIC SOCIETY AND THE CHICAGO NEUROLOGICAL SOCIETY

H. H. Garner, M.D., *President*

Louis B. Shapiro, M.D., *Secretary*

Illinois Psychiatric Society

Douglas N. Buchanan, M.D., *President*

Meyer Brown, M.D., *Secretary*

Chicago Neurological Society

Joint Meeting, April 13, 1954

The first order of business was the presentation of an obituary of Dr. Leo A. Kaplan by Dr. John J. Madden.

Physiologic Aspects of Psychiatric Disorders. Dr. Nolan D. C. Lewis, New York.

Man as an organic unit is integrated by the nervous and circulatory systems into a being possessing, among other functions, the powers of thinking, including judgment, memory, and

speech. The physiologic responses of his anatomical structure are conditioned by, and make adaptations to, the multiple variations of his inherited and acquired constitution and the physical and cultural forces that bear upon him.

Since mental phenomena are so complex and are exceptionally difficult to determine by means of animal experimentation, which has elucidated physiology in other systems of the body, any explanation of disorders in this field on a physiologic basis would undoubtedly require a radical revision sometime in the future.

Various modern studies and leads provide a fairly large amount of evidence for the psychophysiologic unity of the organism; therefore a current concept, namely, that psychological events and disorders have a corresponding differentiation in the physiologic patterns of somatic reactions, may be proved eventually.

Studies during the past 20 years on the structure and functions of the brain and on the relation of other organs of the body to the brain functions have revealed only a fraction of what remains to be done on the primary problems of the mind and its disorders. Approaches to the problem now under way in several research centers include investigations on the neocortex; on the hypothalamic-cortical system with its widespread implications; on adrenocortical functions; on the various shock therapies, including psychosurgery, with their biochemical, metabolic, physical, and psychological changes, and on the experimental psychoses that are now being produced by chemical means for a variety of studies.

Although the scientific understanding of mind and its disorders has had rather modest beginning, it has been placed in its evolutionary framework, and several gaps in knowledge have been closed by experience and experiments.

Neurologic Aspects of Psychic Functions. Dr. J. M. Nielsen, Los Angeles.

Slides were shown of sectioned brains of patients after cerebral lesions and neuropsychiatric symptoms. In Case 1, there were bilateral lesions of the calcarine areas, with total blindness but with perfect recall of visual memories.

In Case 2, the left occipital cortex had been destroyed, and the patient showed visual agnosia for animate objects, with recognition of inanimate objects.

In Case 3, the right occipital lobe was destroyed, with resultant visual agnosia for inanimate objects.

In Case 4, the right occipital lobe was destroyed, with resultant visual agnosia for inanimate objects and with excellent preservation of recognition of animate objects. The patient recognized flowers.

In Case 5, the patient had a lesion subcortical to the left area of Broca, with complete motor aphasia. He recovered his speech in 18 months. Nine years later he had a lesion subcortical to the right area of Broca and, again, motor aphasia.

In Case 6, the patient had a destruction of the left area of Broca and the surrounding area, with complete motor aphasia. She recovered her speech (time required unknown). She was seen five years after the first episode and was speaking as well as ever. She died of cardiac decompensation. An autopsy was performed.

In Case 7, a man had destruction of the left area of Broca but recovered in two years without help.

These cases show spontaneous recoverability from aphasia by means of the opposite hemisphere. They also show that patterns of memory for objects are often located in one occipital lobe for animate objects and in the other for inanimate objects, but that only in the occurrence of a lesion with subsequent autopsy can one determine which is which. These differentiations are infantile, and obviously they are made in the first few years of life and remain for life.

Dreams are chiefly visual hallucinations and depend on the cortex for revisualization. If this is destroyed, dreams cease.

DISCUSSION

Dr. Percival Bailey: Just before I came here, I got a paper from an eminent neurosurgeon, saying that he had repeated the Chicago work in cats and monkeys and was not able to corroborate the results. He is going to present a paper before the American Neurological Society.

There is no question about the existence of the akinetic syndrome, because that has been produced by Magoun and some of his co-workers by using a different technique. The only

argument is as to what structures in the neighborhood produce the syndrome. Dr. Nielsen talks about Areas 17, 18, and 19. There are very drastic disturbances in that portion of the cerebral cortex. There may be no distinct histological difference between Areas 18 and 19, but when the lesions lie closer to or farther from Area 17 there are some differences in the symptoms which result. There is, however, a vast area of the cerebral cortex about whose functions we know little. That does not mean that there are no disturbances caused by lesions in those regions of the cerebral cortex. One does not know what questions to ask these patients. Dr. Nielsen said he did not previously ask them about dreams. Once one knows what questions to ask, one gets information right away. Like the peripheral nervous system, once we learned to tap the knee jerks, we found many useful data. Some day we shall learn what questions to ask these patients with arteriosclerotic disturbances. I am hoping Dr. Simmel will think of what questions to ask patients with temporal lobe lesions. Certainly, I have not learned what questions to ask. Dr. Nielsen continues to work at this problem and, because he has done it, he has thought of new questions. The attention of the psychiatrist is being directed away from the brain. I think we shall have to bring back the attention of the psychiatrist to the brain before we learn what relation there is between psychiatric and cerebral disturbances.

DR. GEORGE PACK, New York: I should like to ask Dr. Lewis whether one can get a change in psychic function without getting disturbances in somatic and physical properties, and vice versa. What is the possibility of those two changes coming simultaneously, one not having any more influence in causing the change than the other, or may they occur simultaneously from one basic cause?

DR. NOLAN D. C. LEWIS, New York: Dr. Pack asked whether one can get a change in psychic function without getting disturbances in somatic and physical properties, and vice versa. I think that theoretically, they are different aspects of the same thing, if one wants to put it that way. They are two different categories, or two different patterns or reactions of the total organism. I think we shall get into difficulty if we speak of cause and effect separately. I did not want to get into that philosophy.

I should like to ask Dr. Nielsen a question on dreams: If some of these patients should say that they have stopped dreaming after this surgical operation, is it a matter of not being able to remember the dreams? There are people who say they never dream. We believe, of course, that they do have dreams but do not remember them. We know people who on waking up know that they have dreamed, but they cannot say what they have dreamed. Then, the dream that is very vivid in the morning at noon is not so vivid. I do not know whether Helen Keller dreams or not.

DR. J. M. NIELSEN, Los Angeles: She was not always blind.

DR. NOLAN D. C. LEWIS, New York: You mean that people who were always blind do not dream? That dream problem is an interesting one. Most of our dream work has been done on children and neurotics, not on normal people.

A field that has not been investigated very well is the whole subject of brain lesions. It includes also the field of aged persons, which has not been investigated well by psychiatrists or psychologists. I do not believe there has been enough work done on psychoneurologic cases as to the nature of the dreams, if remembered. I think we are "missing the boat" on much of our physiological, as well as psychological investigations, by not taking into account some of the things relating to therapy, namely, why some people get well and some do not. A certain percentage react favorably, and others have no effect at all from any kind of therapy. There is a forked-road situation which is ideal from the standpoint of all kinds of experiments.

DR. PERCIVAL BAILEY: Dr. Lewis remarks that there are two types of schizophrenia. What does he think about separating out a group of cases from this vast array that are called by the name of oneirophrenia?

DR. NOLAN D. C. LEWIS, New York: Dr. Bailey asked about separating out a group of cases that are called by the name of oneirophrenia. One might have some difficulty in collecting a very large group for study, as outlined by Meduna and his co-workers. Research on such a group might be revealing. I should like to see research done with all types of somatic and chemical procedures. I should like to see control groups built up of subjects who are suffering from different types of psychoses. Much will have to be repeated because investigators have taken normal persons to compare with sick groups. Anything found chemically or constitutionally,

or in any other way, must be present in some degree in many so-called normal people who carry the disorder as a predisposition. It is not at all satisfactory to compare normal people and persons with different types of psychoses. We get differences in people and differences in other things. If one finds a constitutional factor, it may be only a predisposition.

DR. ROLAND P. MACKAY: I should like to ask Dr. Nielsen to clarify one or two ideas. Can he explain the occurrence of agnosia for animate and not for inanimate objects? Also, how does one classify false teeth as animate? Are we to understand that a lesion in one hemisphere may cause agnosia for animate objects and one in the other hemisphere for inanimate objects? We have heretofore attributed agnosia to lesions in the "dominant" hemisphere. Must we now revise this concept?

DR. PERCIVAL BAILEY: Dr. Nielsen's proposition interests me. Hughlings Jackson was interested in epilepsy. One morning he came to the hospital and asked whether there were any new cases, and the resident replied, "Just another epileptic." Jackson replied, "My boy, there is no such thing as just another epileptic. They are all different." Our residents are very apt to say, "Just another arteriosclerotic." Dr. Nielsen shows that they are all different. One can find out interesting and important things by examining them.

DR. JULES MASSERMAN: I should like to submit to the consideration of our two essayists, first, the production of schizophrenia. I believe we can demonstrate that this can be done by rather severe trauma. One can see a transition in animals from patterns one ordinarily calls neurotic to the production of catalepsy.

As to the nature of Dr. Nielsen's proposition, I should like to have his comment. I agree that the reaction produced can depend just as much on the previous experience of the animal as it can on the locality of the lesion. For instance, a normal animal trained to respond to a certain situation before a lesion in the dorsomedial thalamus will show some postoperative impairment of skill but will remain a friendly animal. In contrast, a neurotic animal treated in the same way will show some impairment and will become a vicious animal. There we have a demonstration as to the importance of the previous experience of the central nervous system in which the lesions are made. Probably from that type of preliminary study in the laboratory we can understand better the effects of various lesions.

DR. J. M. NIELSEN, Los Angeles: In regard to Dr. Lewis' question, whether it may be that the patients merely do not remember the dreams. That may be, but there are patients who remembered their dreams before but do not now. That is as far as I can go. I do not want to project into the future with a little bit of knowledge. We shall need more cases.

With regard to Dr. Mackay's question, namely, that a lesion in one hemisphere will cause agnosia for animate and not for inanimate objects, one can remove one hemisphere with no trouble in some persons, as all patterns are on one side. But if the patterns are divided between the sides, those for animate objects are usually on the side for language. If you want me to project and try to figure out why the patients have this division, I can only say that when an infant first sees an object, he will decide that this is something that has power to move and this other something has not. Patients so far studied classified flowers as animate. I have never yet completed an examination, because one can examine for only a few minutes at a time, as the patient fatigues. So one returns day after day, and before one is through the patient dies or recovers. Our clue to likely cases is homonymous hemianopsia.

What Dr. Masserman said is correct. I acknowledge there are differences in human beings, but I should hate to state on what basis one would make the differentiation.

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY, AND THE NEW YORK NEUROLOGICAL SOCIETY

James H. Wall, M.D., Chairman, Section of Neurology and Psychiatry, Presiding
Joint Meeting, March 9, 1954

Case Presentations of Pseudoneurotic Schizophrenic Patients Treated with Psychosurgery. DR. PAUL H. HOCH, DR. J. LAWRENCE B. POOL, DR. JOSEPH RANSOHOFF, and (by invitation) DR. JAMES P. CATTELL and DR. HARRY H. PENNES.

During the past five years we had the opportunity of observing the results of psychosurgery in a series of more than 40 patients suffering from the pseudoneurotic form of schizophrenia. The operations included topectomy, medial lobotomy, and precoronal lobotomy. All these patients

had a mixture of anxiety, phobic, obsessive, depressive, and hypochondriacal symptoms—a neurotic superstructure masking the primary symptoms of schizophrenia. It was found that 65% of the patients operated upon were significantly improved. On 16 of these patients we have a follow-up of three to five years after operation. In this group of patients 88% show a significant improvement. Our data suggest that improvement after psychosurgery may continue for a much longer period than is usually reported. All the patients operated upon had been sick for several years and had received other forms of psychiatric treatment, such as psychotherapy, psychoanalysis, and shock therapy, without any lasting results. Two patients were presented, and data were discussed which showed no striking relationship between duration of illness or particular symptom constellation and response to psychosurgery, but there is a definite indication of a positive relationship between age at onset of illness and response to operation. The results of this study will appear in a future publication.

DISCUSSION

DR. BURNESS E. MOORE (by invitation): This paper represents a further attempt to clarify the role of psychosurgery in the treatment of mental disorders. In selecting a group of pseudoneurotic schizophrenics for operation, the authors have provided an opportunity for the comparison of the response to psychosurgery of so-called neurotic and psychotic symptoms. They were wise to choose those patients who were more heavily weighted on the psychotic than on the neurotic side. This factor should be of some theoretical, as well as practical, value, since we still do not fully understand the differences and similarities in the evolution of these two groups of symptoms. Unfortunately, we are also often at a loss as to how to bring about even partial social recovery in this type of patient after prolonged psychotherapeutic attempts have failed. The demonstration that psychosurgical procedures afford a high degree of significant improvement without accompanying damage to the personality is exceedingly worth while. However much we may hope in the future to attain the psychological means of curing these patients, we have to accept the fact that for the present such means are largely unavailable.

All of us are having a great deal of difficulty in understanding why some patients improve and some do not. We are very hesitant to operate on a patient who has hypochondriacal symptoms that seem to mask an underlying schizophrenic process, because that patient is utilizing his defenses effectively and seems to be functioning at the best level of which he is capable. Psychosurgery under such circumstances may disturb his integration and bring out a severe underlying psychosis.

DR. PAUL H. HOCH: We did not start out with psychosurgery in this group of patients. That treatment was not the first type. These patients all had psychotherapy for a long time. The pseudoneurotic group of schizophrenics responds to psychotherapy in 20 to 25% of the patients. These patients do not respond to shock. Actually, they sometimes become worse with shock because it increases their anxiety very much. We believe that if patients fail with psychotherapy, they should not be treated for 10, 15, or 20 years, as sometimes happens with different psychotherapists, because today with psychosurgery many of these patients are relieved of their symptoms.

I should like to call attention to the very widely ramified symptomatology of the patients I presented, which shows how a great degree of tension and anxiety produces different symptoms. The operation relieved not only the anxiety of the patient but also the other symptoms. These patients are an ideal group for operation, and I believe if they do not respond to psychotherapy, they should be subjected to this smaller form of psychosurgery, which has not damaged them but has relieved the symptoms considerably in many patients.

Neurologic and Psychologic Factors in the Total Body Experience. DR. HANS OPPENHEIMER (by invitation).

The concept "total body experience" is suggested as an extension of the original idea of a body image. The various components constituting the total body experience are tentatively relegated to more or less distinct systems of integration and include the following: 1. Awareness of posture and movement, the "postural model" in the narrow sense of Head. 2. Awareness of

spatial relationships of body parts (body orientation), with its linkage to language function, clinical manifestations of lesions: autotopagnosia, Gerstmann's syndrome. 3. Awareness of extrapersonal space, an extension of the directional body image. 4. The experiencing of body parts as being parts of the self, as belonging to the self. This functional component seems to be mediated through thalamoparietal circuits. Lesions may cause periodic neglect, feeling of estrangement, illusion of absence, and amnesia of the contralateral (left) half of the body, with or without psychopathologic elaborations and distortions (somatoparaphrenia). 5. A system mediating the awareness of certain basic ego functions (motility, vision, hearing) via thalamocortical circuits. Lesions within this system may be a factor in the causation of imperception of central blindness and deafness and of anosognosia of (left) hemiplegia.

An evaluation of the factors leading to the denial syndrome is attempted, and a distinction is suggested between imperception and denial of defects; the former is presumed to result from a neurologic defect; the latter, to serve a psychologic purpose. Accordingly, the entire question of "anosognosic focus" versus "anosognosic personality" is reexamined. It is believed that such an alternative formulation constitutes a pseudoproblem.

The relationship between perceptual impairment (predominantly "neurologic") and wish to deny illness (predominantly "psychologic") will determine the final clinical picture: Perceptual impairment within the total body experience will facilitate denial, and the more pronounced this impairment is the greater the characterologically determined tendency toward denial of illness is. The term anosognosia should be restricted to the imperception or denial of basic ego functions (motility and distance perceptors). The specific perceptual element in the total body experience may be impaired at various "levels," as follows: (*a*) diffuse perceptual impairment due to general lowering of the acuity of the perceptual apparatus in diverse brain disease; (*b*) elimination of body territories or central sensual spheres from awareness due to thalamocortical lesions, and (*c*) a specific perceptual abnormality consistent with frontal lobe impairment, resulting in failure to comprehend the significance to the patient of his defect.

In the absence of any form of perceptual impairment it is doubtful whether the central wish to deny illness will ever be strong enough to lead to imperception of basic defects short of psychotic denial of reality within the total body experience.

DISCUSSION

DR. JOSEF GERSTMANN (by invitation): The concept of the body image, or body scheme, or postural model of the body has not received much attention among neuropsychiatric workers for many years. It was not until recent years that this concept gained increasing interest in neurologic and psychiatric circles. There is, however, still a relative scarcity of adequate contributions to the subject. Dr. Oppenheimer's proposition of a so-called "total body experience" deserves further, more specific study.

The best approach to the study of the body image and its disorders seems to me the clinical-phenomenologic one, with due elaboration of their neurologic and psychologic aspects. From this standpoint there appears to be most feasible the following classification of the diverse manifestations of body disorientation referable to the body image: (1) direct disorders of the body image, as a rule bilateral, due to affection of the dominant cerebral hemisphere, and (2) indirect disorders of the body image, usually unilateral, due to affection of the nondominant hemisphere. The first group comprises (*a*) general disorientation and lack of recognition in the sphere of the body and in the interrelation of its individual parts, one's own as well as those of other persons, known under the name of autotopagnosia (Pick). The author prefers to name it somatotopagnosia; (*b*) primary specific disorientation and lack of recognition in the sphere of the fingers of both hands and in their spatial relationship, one's own as well as those of others, known under the name of fingeragnosia (Gerstmann), and (*c*) disorientation and lack of recognition for right and left in the sphere of the body, one's own as well as that of others (usually associated with either of the two conditions just mentioned). The second group comprises (*a*) lack of knowledge of disease, most frequently observed with left cerebral hemiplegia, known under the name of anosognosia (Babinski), and also observed in cortical blindness and cortical deafness; (*b*) amnesic and agnostic unawareness of the impaired parts or side of the body, varying in degree from simple neglect or denial of their presence to the experience of their nonexistence, termed by me autosomatamnesia and autosomatognosia, respectively, and (*c*) specific psychic elaboration

(marked by formation of illusions, confabulations, and delusions) with respect to the defective members or side of the body, believed or experienced as absent, termed by me somatoparaphrenia.

DR. EDWIN A. WEINSTEIN: This paper has been a thoughtful one, in which there has been an attempt to bring a large mass of clinical data into a meaningful system, designated as "body experience." One's ideas of the "body scheme" or "body image" depend on what one is trying to explain, and one's ideas are determined by the types of cases seen, by the methods of study that are used, and by certain a priori beliefs of the observer. Thus, the body image has been evoked in describing such varied phenomena as vertigo, phantom limb, confusion between right and left, denial of hemiplegia, and delusions of reduplication of parts of the body. The subject is tremendously important, I think, and these cases ought not to be regarded as merely bizarre neurologic curiosa. They furnish important clues as to what happens after prefrontal lobotomy and electric shock, and also relate to the whole problem of the relationship of perception and symbolic formation in language.

DR. HANS OPPENHEIMER: What I was mainly interested in, as can be seen from the title, was to evaluate the relative role of so-called neurologic and psychologic factors in this particular area, which I have called the total body experience. This evaluation is not meant as an alternative formulation of the problem, for in each individual case an attempt must be made to evaluate the question to what degree focal and nonfocal factors contribute to the final clinical picture.

Finally, as far as the evaluation of neurologic and psychologic factors in any condition is concerned, I should like to quote Dr. Kubie in a remark which seems not inappropriate to be mentioned in this gathering, that he was looking forward to the time when the shades of Freud and of Cushing would shake hands!

An Antiepinephrine Factor in Treatment-Resistant Schizophrenic Patients. DR. LEO ALEXANDER (by invitation), Boston.

A recent study of the prognostic significance of the epinephrine-methacholine (Mecholyl) test (Funkenstein test) in demonstrating the role of exaggerated or deficient autonomic responses in prognosis revealed that the markedly reduced response to epinephrine that is characteristic of Funkenstein's Group V makes this the most unfavorable prognostic one of all. The differences between all reaction groups were found to be statistically significant at the 0.03 level. Inspection of the data made possible by a $2 \times k$ chi-square analysis revealed that Group V, as the most unfavorable group, was the greatest contributor to this difference. Most of the patients falling into this group were schizophrenics; a few were chronic neurotics, probably better classified as pseudoneurotic schizophrenics, and a number had chronic psychalgic states, with or without overt depressive features. Prior to the present study I had found that patients showing such reduced response to epinephrine did not respond to any treatment except insulin coma. In the two instances in which full recovery had resulted from insulin coma therapy, the response to intravenous injection of epinephrine became normal when they recovered clinically.

The present study is an attempt to study the physiologic characteristics of reduced response to epinephrine. On injection of 0.025 mg. of epinephrine, the blood pressure of most normal subjects will rise 30 to 70 mm. Hg, the average being about 50 mm. Hg. For the purposes of this study, markedly inadequate response to epinephrine has been defined as a blood pressure rise of less than 20 mm. Hg upon intravenous injection of the above-stated amount. It was found that atropinization, as well as administration of cortisone or corticotropin, counteracted the inadequacy of response to epinephrine, suggesting that this inadequacy of response is probably caused and maintained by an antiepinephrine factor of cholinergic, muscarinic nature, which can be counteracted by atropine, as well as by the production of a hyperadrenal state. Two patients in whom the response to epinephrine became normal on corticotropin therapy showed marked clinical improvement. One of these had failed on all other forms of treatment, while one had had no previous treatment. In the former the clinical improvement and the improved response to epinephrine outlasted the period of corticotropin therapy. The other patient relapsed on discontinuance of corticotropin. These preliminary experiences warrant more extensive therapeutic trial of corticotropin in patients exhibiting this type of autonomic reaction pattern.

DISCUSSION

DR. DAVID J. IMPASTATO: The work of Dr. Alexander, and also of Drs. Funkenstein, Greenblatt and Solomon, may help us in sharpening our diagnostic abilities, because they have added, to the usual historical, physical, and mental studies of reaching a diagnosis, easily obtained autonomic responses. If this work is fully corroborated, our psychiatric diagnoses may become more definitive. Their work may also help us to select a more specific type of treatment for our patients. Until recently our indications for a specific type of treatment have not been very clear. With the help of the autonomic responses, the indications are clarified, at least to some extent.

Dr. Alexander has advanced the findings of Funkenstein and his collaborators, and his work supports the latter's postulate that changes in the psyche are accompanied by physiologic changes. The autonomic changes described by Dr. Alexander are just one aspect of the possible changes that might occur in the body before and after treatment. Changes in the steroid excretion, in the blood, in salivation, in electrical responses of the brain, etc., have been described. I believe that eventually, when all these changes have been correlated, we may be in a better position to diagnose and treat the patient.

DR. LEO ALEXANDER: The question as to which patients secrete an excessive amount of epinephrine or arterenol, respectively, has to be evaluated on indirect evidence. Epinephrine does not counteract the muscarinic effect of acetylcholine. Therefore, a drug like methacholine will depress the blood pressure, as in Funkenstein's Types VI and VII. Arterenol, on the other hand, does counteract the muscarinic effects of acetylcholine, hence the blood pressure will not fall significantly, and may even rise, on injection of methacholine because of its nicotinic-adrenergic effect, such as occurs in Funkenstein's Types I, II, and IV. In the types of cases which were the subject of my paper, in which the blood pressure failed to rise adequately on intravenous injection of epinephrine, we have no evidence as to whether or not the patients actually secrete inadequate amounts of epinephrine or arterenol. I believe, however, that I have presented conclusive evidence that their capacity to respond to intravenously injected epinephrine is blocked or counteracted by an antiepinephrine factor, probably of cholinergic-muscarinic nature.

James H. Wall, M.D., Chairman, Section of Neurology and Psychiatry, Presiding

Joint Meeting, May 11, 1954

Acute Cerebral Venous Occlusion Manifested by Spontaneous Subarachnoid Hemorrhage. DR. STEFAN SZANCER (by invitation).

A 45-year-old man was admitted to hospital with a few days' history pointing to an acute vascular disorder involving predominantly the left cerebral hemisphere. Lumbar puncture yielded a grossly bloody spinal fluid. The patient had a past history, extending over a period of 20 years, of venous thromboses involving the lower extremities and of episodes of mesenteric thrombosis and pulmonary infarction.

Autopsy revealed a subarachnoid hemorrhage with hemorrhagic destruction of the left temporal lobe due to thrombosis of the left middle cerebral vein.

Literature dealing with the subject of noninfectious intracranial venous thrombosis was briefly reviewed.

Psychopathologic Indications and Contraindications for the Use of Subcoma Insulin Treatment. DR. DONALD C. GREAVES (by invitation).

In distinction to the accepted definition of coma insulin therapy, the status of coma insulin therapy is still unclear. From 1942 to 1952 coma insulin therapy, at New York Hospital-Payne Whitney Psychiatric Clinic, was considered to be that which produced a hypoglycemia sufficient to cause clouded consciousness for 45 to 60 minutes, stopping short of coma. This procedure was used in the treatment of 212 patients. There was improvement in 79.6% of 133 schizophrenic patients. Those psychopathologic reactions most favorably affected were catatonic excitements with marked fear, depression, or elation; acute paranoid reactions with fear, incoherence, depression, or elation, and schizophrenic episodes of excessive anxiety. In contrast to those patients with

schizophrenic illnesses, patients with affective illnesses did not do better when severe anxiety and fear were predominant. Patients with elation and anger, sexual excitement, or resentment and panic all responded well. Treatment was evaluated on the basis of psychopathologic examinations at the initiation and termination of treatment. No attempt was made to evaluate results of treatment in terms of the condition at discharge from the hospital, since it was felt that this would give a misleading picture of the usefulness of this form of treatment. It is felt that many distressing symptoms can be controlled or relieved by subcoma insulin therapy without necessarily altering the basic underlying illnesses.

Schizophrenic Children Under the Age of Six Years. DR. MANUEL FURER (by invitation).

Two schizophrenic children from the nursery of the Children's Service of Bellevue Psychiatric Hospital were presented to demonstrate what are considered to be reparative attempts to deal with the deficiencies in adaptation that result from the characteristic lag in maturation of the ego. The preoccupation with the surface of their bodies and with distant sense perception is felt to represent, in part, an effort to deal with an incompletely established body image and separation of the self from the not-self. The early rigidity and compulsiveness in their behavior, described by Kanner as a demand for sameness, and sometimes including impulsions, as described by Bender and Schilder, are thought to represent, in part, an attempt to deal with an external world conceived as chaotic. This conception arises partly out of the defect in differentiation of the self, as well as the projection of a sense of internal disorganization, and perhaps, also, direct disturbances in perception. It was pointed out that these preoccupations appear transiently in the normal development of the infant at a time when similar problems are being dealt with by the maturing ego—the body image problem under one year of age and the problem of the control and organization of impulses, beginning between 1 and 2 years of age.

Survey of General Surgical Procedures in a Group of Emotionally Disturbed Women Patients. DR. WILLIAM A. TRIEBEL (by invitation).

The difficulties encountered in diagnosing organic pathology requiring surgical intervention in emotionally ill persons were discussed. The case of a 26-year-old nursery-school teacher, who was operated upon for what appears to have been psychogenic vomiting, was presented.

A review of previous surveys of this topic was made, with a criticism of the adequacy of their control studies. The results of a survey of 300 women patients at New York Hospital-Westchester Division, with a control group matched with respect to age and marital and socioeconomic status, were presented.

The main findings were as follows:

1. The surgical rate among patients was 43%; in the controls, 28%.

2. The psychoneurotic group had a surgical rate of 65%; the matched controls, 23%.

3. Each diagnostic category had a surgical rate significantly higher than the controls, with the exception of the dementia praecox group, in which the rate was not significantly higher than the control group.

4. Patients tended to have multiple procedures.

5. In the patients in all diagnostic categories, gynecological and rectal procedures made up 44% of the operations, but made up only 20% of the operations in the control group.

Several hypotheses were offered to explain these differences, and some suggestions were made to the end of avoiding surgery for emotionally determined symptoms.

The Creative Drive: A Case History. DR. RICHARD S. BLACHER (by invitation).

The artist has always enjoyed a special position in society, in part due to the unusual nature of his inspiration. He has been thought to create by reason of divine influence. Through the ages philosophers have speculated on the basis for artistic creativity, and in recent years the creative drive has come under study by psychiatric workers. The sublimation of sexual and infantile impulses, the need to turn from reality, the desire to control, and the wish to share guilt with others have all been mentioned by psychiatric writers. The relationship of artistic creation to biologic creation in both men and women has been pointed out. A case history is

presented which, it is believed, demonstrates the sublimation of the biologic creative drive by means of artistic creativity. Further, it is shown how both types of creativity may be utilized as a defense against the fear of impending death or disaster. The patient is a 39-year-old woman who was successively a singer, actress, sculptor, writer, poet, and photographer, but who was dissatisfied with each artistic endeavor. Although unmarried, she decided to have a child. In her eighth month of pregnancy she developed a depression and was hospitalized. She talked freely of her early rejection by her mother, about identification with her father, and of strong homosexual tendencies. When she went into false labor, she became panicky and told of a story she had once written about a woman who kept herself from committing suicide by means of frantic creativity, only to die in the end. When the patient is seen in the light of her own story, it would appear that this magical warding off of death is the motivation for the patient's own creativity.

DISCUSSION ON PRECEDING PAPERS

DR. S. BERNARD WORTIS: With regard to Dr. Szancer's paper, migratory phlebitis is an interesting syndrome, which was described by Osler. This condition may be related to the development of an organic mental syndrome. I have seen a patient with this clinical picture.

Dr. Greaves gave confirmatory evidence to support reports from other clinics and emphasized that the prominence of affective coloring in a schizophrenic improves his prognosis. I should like to know what Dr. Greaves meant when he indicated that they used psychopathologic criteria other than the usual diagnostic labels. Perhaps he will describe for us more specific psychodynamic changes that he intimates were used in evaluating these patients.

Dr. Furer focused on the importance of recognizing the obsessive-compulsive syndrome in earliest childhood, together with changes in the body image psychology. This occurrence has been stressed by Bender and others, and suggests that there is a biologic basis for childhood schizophrenia. Dr. Lauretta Bender has also stressed the presence of "soft" neurologic signs as evidence of disturbance in neuromuscular patterning.

Dr. Triebel points to the polysurgical addict, the emotionally disturbed patient. As I was listening to Dr. Triebel, I could not help feeling that our teaching of undergraduate medical students must be unsatisfactory, because we do not alert future physicians enough to these problems.

Dr. Blacher described the psychobiologic creative drive in the artist and how in his patient pregnancy represented a drive to create. We see in Bellevue many cases of girls who are pregnant, in which I think other biologic drives, rather than the artistic one are in action.

DR. M. RALPH KAUFMAN: As Dr. Greaves pointed out, as one looked at the various categories, one was reminded of practically every type of case that had ever been presented in terms of improvement. Dr. Greaves made the point that he was talking about improvement of specific symptoms at the time, rather than improvement of the total situation. He also related the use of subcoma insulin treatment to intensive psychotherapy.

Dr. Furer presented the Bellevue point of view in regard to childhood schizophrenia; the Bellevue group, especially Dr. Bender, has been in the forefront in the delineation of this particular category.

Dr. Triebel pointed out one aspect of the situation, that psychiatric patients, by and large, seem to have more operations than nonpsychiatric patients. Ideally, every psychiatrist likes to feel he does not make a diagnosis by exclusion. On occasion, a diagnosis of no organic disease is made and the psychiatrist is able to point out that there must be organic disease present.

DR. BERNARD C. MEYER (by invitation): Dr. Triebel has spoken of surgical problems arising among psychiatric patients. The converse, too, is a rich and interesting field, namely, the psychiatric complications of surgical patients. There are patients who approach surgery with a conviction that they will die, a state of mind which must be distinguished from the commoner fear of death. Experienced surgeons tend to shy away from operating upon patients possessed of such gloomy forebodings because, on occasion, they have come true.

Dr. Blacher's patient provided a most fascinating study, embracing psychologic aspects both of pregnancy and of creative art. It is clear that this young woman was compulsively pursuing in vain one artistic expression after another and always failing to achieve her goal. It is also obvious that a basically self-destructive aim underlies her entire life story.

DR. JOSEPH W. OWEN: Dr. Greaves' paper on the use of subcoma insulin reminds me that in military service acute panic was a difficult problem to handle. These panics occurred in good, conscientious men who under long strain and great stress developed marked excitement with delusions, and occasionally some hallucination. These states lasted generally one to three weeks. We tried every type of sedation we could, and we seemed to do very little for them, until someone suggested subcoma insulin. The results often were very dramatic. I should think further experimentation with this method might be indicated in various excited wards.

DR. DONALD C. GREAVES: We did not have any detailed information on the different groupings from the standpoint of psychodynamics.

Dr. Kaufman emphasized that the impression was based on the patient's state at the completion of insulin therapy and had little correlation with the state at the time of discharge from the hospital. Many patients were in the hospital for weeks and months after the completion of their insulin treatment.

DR. WILLIAM A. TRIEBEL: I did not intend to leave the impression that I felt this increased surgical rate was entirely due to needless operations; we do not have enough evidence in this survey to say that. Probably a proportion of these cases do represent people who had no pathology. Operation proneness is probably due more to anxiety and body overconcern than to conversion.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Physiology and Biochemistry

CEREBROSPINAL FLUID PRESSURE AS AN AETIOLOGICAL FACTOR IN THE DEVELOPMENT OF LESIONS AFFECTING THE CENTRAL NERVOUS SYSTEM. J. E. A. O'CONNELL, Brain **76**:279 (June) 1953.

O'Connell presents observations on the fluctuations in cerebrospinal fluid pressure occasioned by postural alterations and by variations in the arterial and venous pressures within the cranium and spinal canal, indicating that the variations in pressure are much more pronounced than is commonly supposed and provide a force sufficient to produce lesions affecting the central nervous system.

Because of the close relationship existing between the cerebrospinal fluid and the systemic venous pressure, it appears that in the absence of any intracranial disease a rise in intracranial venous pressure may produce gross signs of increased intracranial pressure, or sometimes focal neurological disturbances. In patients with chronic bronchitis and emphysema the marked and repeated increases in intracranial pressure produced by coughing and raised systemic venous pressure appear to explain the occurrence of papilledema and retinal hemorrhages.

The cerebrospinal fluid pulse, especially when superimposed upon the considerable hydrostatic pressure in the lower portion of the dural theca, appears to provide a force adequate for the development of cystic dilatations of the subarachnoid space; they may be entirely intradural, the cyst wall being composed of arachnoid only, or they may have an additional dural envelope, so that an intraspinal meningocele is produced.

The normally subatmospheric intracranial pressure in man is hypothesized as a factor in the production of chronic subdural hematoma, so that a minor head injury which brings the lumen of an intracranial vein into continuity with the subdural space will be more likely to be followed by a hematoma than a severe injury, after which intracranial pressure will be raised by laceration, contusion, and edema of the cerebrum. Also, the long latent period between injury and development of the typical clinical picture may be due to the fact that blood collecting in the subdural space is producing no compression—it simply permits the collapse of vascular and subarachnoid channels previously held open by the subatmospheric intracranial pressure. It is also suggested that production of the hematomata is secondary to withdrawal of the arachnoid villi from the lateral lacunae of the sagittal sinus, leading to rupture of the vessel and opening the subarachnoid space into the subdural one, thus accounting for the usually observed contents of the hematomata.

JOHNS, New York.

CREATINE AND GUANIDOACETIC ACID METABOLISM IN MUSCLE DISEASE. J. N. CUMINGS, Brain **76**:299 (June) 1953.

Cumings reports the results of examination of the urinary creatine, creatinine, and guanidoacetic acid; of the blood levels of creatine and creatinine, and of creatine tolerance tests in 67 cases of muscular abnormalities. Normal results are present in myotonia congenita, in some cases of myasthenia gravis, and in myopathic ophthalmoplegia. Creatinuria is present in myotonia atrophica, myasthenia gravis on neostigmine (Prostigmin), muscular dystrophy, neuronopathy, dermatomyositis, and porphyrinuria. The creatine tolerance is grossly diminished in myotonia atrophica and in generalized muscular dystrophy only. Guanidoacetic acid, a precursor of creatine, is normal in all mucular disease, but in two cases of polyneuritis associated with porphyrinuria there are extremely low excretions, along with a marked creatinuria.

JOHNS, New York.

EFFECT OF ACUTE ALCOHOLIC INTOXICATION ON THE BLOOD-BRAIN BARRIER. W. J. HORSEY, J. Neuropath. & Exper. Neurol. **12**:368 (Oct.) 1953.

Cats were administered ethanol in acute and chronic preparations. There was no change in the hematoencephalic barrier as tested by trypan blue, fluorescein, and copper phthalocyanine.

SIEKERT, Rochester, Minn.

ESTERASES AND PHOSPHATASES OF THE BRAIN. G. GOMORI and R. D. CHESSICK, J. Neuropath. & Exper. Neurol. **12**:387 (Oct.) 1953.

The authors report their histochemical method and observations on the demonstration of esterases and phosphatases in the central nervous system of the dog and rat. For the demonstration of the esterase two substrates were used, alpha-naphthol acetate and naphthol-AS acetate. The results obtained from these substrates showed marked differences in the distribution pattern of activity. For the demonstration of phosphatases, two substrates were also used: glycerophosphate for nonspecific alkaline phosphatase and muscle adenylic acid at pH for 5-nucleotidase.

In the dog the alpha-naphthol method for demonstrating esterases may stain well-defined fiber tracts and nerve cells. The nerve cells show several morphologic patterns: completely unstained, staining of the surface of the nerve cells, or staining of the entire cytoplasm. Intense staining was observed in the anterior horns, the inferior olives, the floor of the fourth ventricle, the cerebellar nuclei, the substantia nigra, the red nucleus, and the nucleus of the third nerve. With the naphthol-AS method all neural staining was in the cytoplasm of the nerve cells and of scattered glial elements. With this method there was intense staining under the ependyma of the fourth ventricle and of the cells of the dorsal nucleus, the trapezoid nucleus, the substantia nigra, the habenular nuclei, and the cornu ammonis.

The records obtained with the phosphatase when using the two substrates were essentially similar. The activity was localized much less selectively with the phosphatase methods than with the esterase methods. In general, all capillaries were intensely stained. The parenchyma in areas of gray matter was much more intensively active than that in the white matter.

In the rat brain the alpha-naphthol method indicated that the activity was predominantly cellular, with the cell bodies diffusely stained. The multipolar ganglion cells in the anterior horns and elsewhere were very active. Moderate staining was seen along the floor of the fourth ventricle and in the area of the olives. Intense parenchymal staining with relatively little cellular activity was seen in the habenular nucleus, the lateral nucleus of the thalamus, and the anterior paraventricular hypothalamic nucleus. All cerebellar nuclei exhibited intense cytoplasmic staining. With the naphthol-AS method the cell bodies stained with greatest intensity. Throughout the spinal cord and brain stem practically all nerve cell bodies, whether motor or sensory, were stained. The cerebellar nuclei, lateral nucleus of the thalamus, habenular nucleus, and reticular nucleus of the diencephalon were positive.

The distribution of alkaline phosphatase and 5-nucleotidase activities differed from each other in that the former was associated with a morphologically undefinable parenchymal substance, while the latter was localized mainly in axons and glial fibers.

Alpha-esterase was inhibited by diisopropyl fluorophosphate (DFP) and partly by physostigmine and by tetraethylpyrophosphate (TEPP). AS esterase appeared to be practically insensitive to DFP, TEPP, and physostigmine.

The nature of the enzymes demonstrated by naphtholic substrates is not clear, and it is altogether questionable whether a sharp and meaningful line can be drawn between cholinesterases and aliesterases.

SIEKERT, Rochester, Minn.

INTRATHECAL INJECTION AND CORTICAL APPLICATION OF CHLORAMPHENICOL. J. W. HANBERY and C. AJMONE-MARSAN, J. Neuropath. & Exper. Neurol. **13**:297 (April) 1954.

Experiments were carried out with chloramphenicol and other antibiotics on cats. Repeated cisternal injections of sterile chloramphenicol solution produced no untoward effects. No gross abnormalities were observed in the central nervous system, and microscopic examination showed only slight thickening of the leptomeninges over the base of the cerebral hemisphere, but other-

wise there were no inflammatory or degenerative changes anywhere. Direct application of the powdered drug to the cerebral cortex caused a transient depression of electrical activity with rapid recovery. No epileptiform waves were noted in the electroencephalogram. When applied to the somatosensory and primary auditory cortex, there was a noticeable increase in the amplitude of evoked potentials, suggesting an increase in the local excitability of the cerebral cortex. Powdered chloramphenicol applied over the cerebral cortex in chronic experiments showed only minor electrical irregularities and no epileptiform activity in the electrocorticogram. Histologic examination of these areas disclosed only slight thickening of the piarachnoid membrane, without definite neuronal change.

Pencillin, streptomycin, bacitracin, neomycin, and erythromycin had epileptogenic properties when applied to the cortex in sufficient concentration. Chlortetracycline (Aureomycin) and oxytetracycline (Terramycin) (each solution contained a small amount of sodium glycinate) caused a marked depression of the spontaneous electrocortical activity but had no epileptogenic properties; cortical damage was severe. Polymyxin B had no epileptogenic properties and did not damage the cortex grossly, but produced a depression of spontaneous electrocortical activity.

SIEKERT, Rochester, Minn.

Neuropathology

ENCEPHALOPATHY PRODUCED BY EXTRACTS OF EOSINOPHILS AND BONE MARROW. J. S. MEYER and J. M. FOLEY, J. Neuropath. & Exper. Neurol. **12**:349 (Oct.) 1953.

A leucocyte cream was obtained by centrifugation of venous blood of patients with leucocytosis and eosinophilia. After dilution with broth, part of the material was passed through a Seitz filter and part dialyzed against water. The bone marrow (human) was extracted with broth and later fractionally precipitated by adding ammonium sulfate. Guinea pigs were inoculated intracisternally or subcutaneously. Cats were inoculated intracerebrally.

In the guinea pig the resulting neurologic syndrome was apparent in several days and consisted of slowness to absence of righting responses. In the severely affected, death rapidly ensued. In all guinea pigs with clinical signs there was affection of the Purkinje cells, varying from fragmentation of the nucleus to complete disappearance, leaving empty baskets with proliferation of the Bergmann astrocytes. Though the cat showed no clinical signs, mild Purkinje cell changes were seen.

The experiments point out that this encephalopathologic reaction, in the "Gordon phenomenon," can also be obtained in guinea pigs by subcutaneous injection, and that in cats neuronal degeneration may be seen without clinical signs.

The chemical identity of the agent remains unknown, but it appears to be of high molecular weight, a protein passable through a Seitz filter and not dialyzable. It appears to be related to the eosinophiles.

SIEKERT, Rochester, Minn.

EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS DURING AND FOLLOWING CORTONE [CORTISONE] ACETATE TREATMENT. A. FERRARO and L. ROIZIN, J. Neuropath. & Exper. Neurol. **12**:373 (Oct.) 1953.

Allergic encephalomyelitis was induced in guinea pigs by Freund's original procedure. Cortisone was administered before, during, and after the development of the encephalomyelitis. If given early, this drug appeared to delay the development and to decrease the intensity of both the clinical symptoms and the inflammatory pathologic reaction.

SIEKERT, Rochester, Minn.

NIGROPALLIDAL ENCEPHALOMALACIA IN HORSES ASSOCIATED WITH INGESTION OF YELLOW STAR THISTLE. D. R. CORDY, J. Neuropath. & Exper. Neurol. **13**:330 (April) 1954.

The entity under discussion, commonly called "chewing disease," occurs in horses in Northern California. The condition has also been called "star thistle poisoning," although this etiological inference has not been verified. The onset of the symptoms was always sudden, with variable

impairment of eating and drinking. The horses showed hypertonia of the muzzle, idle chewing and tongue flicking, lethargy, and slow gait. All the cases occurred in association with pastures heavily grown with yellow star thistle (Centaurea solstitialis).

Neuropathologic investigation showed bilateral symmetrical foci of necrosis or softening in the anterior portion of the globus pallidus and the substantia nigra. The foci varied in appearance according to their duration. The early lesions were distinct, but not sharply outlined, and slightly yellow. Later these foci became paler, sharply demarcated, and distinctly soft. Chronic lesions appeared as cavities filled with semifluid contents. Microscopic lesions showed sharply outlined necrosis with subsequent liquefaction. Later there was surrounding astrocytic proliferation.

Three experimental horses were fed a diet containing yellow star thistle, and at autopsy similar pallidal foci were seen. No transmissible agent could be demonstrated. No counterpart of this entity could be found in the veterinary literature, and its comparison with certain human conditions and possible causative mechanisms are discussed. These included parkinsonism and related conditions; the familial syndromes of Hallervorden and Spatz, Kalinowsky, and Winkelman; carbon monoxide poisoning and other anoxic conditions, and pallidal siderosis.

SIEKERT, Rochester, Minn.

THALAMIC PATHOLOGY OF AMAUROTIC FAMILY IDIOCY: CONTRIBUTION TO THE CYTOLOGY OF THE THALAMUS. L. H. LEMIEUX, J. Neuropath. & Exper. Neurol. **13**:343 (April) 1954.

Lemieux reports studies on the pathology of the optic thalami in two cases of amaurotic family idiocy which occurred in identical twins, beginning at the age of 4 and lasting for five years. The typical nerve cell changes, with marked swelling of the nerve cells, with displacement of the nucleus and partial to complete tigrolysis, and with much abnormal lipoidal material within the cytoplasm, are recalled. From the cytologic investigation it appeared that the intralaminar nuclear system appeared to be more diffuse than is generally realized. The nuclei with subcortical connections are composed of neurons of a single type, none of which showed vacuolar changes. Of the cortical relay nuclei, the anterior nucleus contained only vacuolated neurons and small nerve cells; the ventral nuclei, exclusive of the anteroventral nucleus, contained three types of nerve cells with few vacuolated neurons. All the association nuclei showed vacuolar changes and some loss of nerve cells. Many of the thalamic nuclei contained a distinct type of small neuron which is not found in the intralaminar system, the midline nuclei, the reticular nucleus, and the medial and lateral geniculate bodies. In general, the neurons of the centromedian nucleus were less affected than those of the anterior medial and lateral nuclei, in which the neurons were fewer in number and contained giant vacuoles with large lipoidal inclusions.

SIEKERT, Rochester, Minn.

Meninges and Blood Vessels

IPSILATERAL THIRD CRANIAL NERVE PALSY AS A PRESENTING SIGN IN ACUTE SUBDURAL HAEMATOMA. E. S. CLARK and W. GOODDY, Brain **76**:266 (June) 1953.

Clark and Gooddy report two cases of acute subdural hematoma with an ipsilateral third cranial nerve paralysis as the only definite abnormal neurological sign. Each case was accompanied by headache of sudden onset. A review of the literature reveals only one similar case. Emphasis is placed on the fact that the clinical picture of headache of sudden onset, vomiting, drowsiness, and a third cranial nerve paralysis may be due to a subdural hematoma secondary to mild head trauma, or that it may be due to a ruptured intracranial aneurysm and the latter may be accompanied by a subdural hematoma. It is observed that angiography should reveal the pressure of a subdural hematoma, and, perhaps, the associated aneurysm as well.

JOHNS, New York.

Diseases of the Brain

MEGALENCEPHALY ASSOCIATED WITH HYALINE PAN-NEUROPATHY. L. CROME, Brain **76**:215 (June) 1953.

Crome records the case of a child in whom convulsions began at the age of 4 months, with enlargement of the head but no evidence of increased intracranial pressure, followed by mental retardation, generalized rigidity, and opisthotonos. The child died at 26 months of age. Pathologically, there was megalencephaly, localized dilatation of the lateral ventricles, spongy degeneration of the white matter, and loss of nerve cells and glial proliferation in the overlying cortex. Similar changes were found in the basal ganglia. Numerous hyaline bodies were found throughout the central nervous system and available proximal portions of the spinal and cranial nerves, being especially dense in the subpial zone of the cortex, brain stem, and spinal cord, around the blood vessels, and in the area of the subarcuate fibers of the centrum semiovale. These bodies stained similarly to fibrin and fibrinoid material, except that they were negative to periodic acid-Schiff stain and were only partially argyrophilic. It was suggested that the hyaline bodies were formed as a result of interaction between the formed tissue elements in the brain and nerves with the "ground substances" or with the derivatives of the cerebrospinal fluid or plasma. It was believed that the case fell into the group of secondary megalencephaly.

JOHNS, New York.

Peripheral and Cranial Nerves

ELECTRICAL METHODS IN DIAGNOSIS AND PROGNOSIS OF PERIPHERAL NERVE INJURIES AND POLIOMYELITIS. C. B. WYNN PARRY, Brain **76**:229 (June) 1953.

Parry reports the results of his experience with electrodiagnostic methods in cases of peripheral nerve injuries and poliomyelitis, involving 72 patients in the R. A. F. The results showed a definite pattern of electrical events in recovery from such lesions, and the use of the strength duration curves (chronaxie) and electromyography were of considerable help in the diagnosis of reinnervation and assessment of ultimate functional recovery. The earliest signs of reinnervation on the strength duration curves appeared about six weeks before the first signs of clinical recovery; on the electromyogram, about eight weeks before. In the majority of cases a diagnostic stimulator (for chronaxie studies) can afford sufficient information for all practical purposes, and the refinements of electromyography are seldom essential. However, in the differential diagnosis of lower motor neurone lesions the EMG is preeminent, for the strength duration curve is merely an assessment of the proportion of innervated to denervated muscle fibers, whereas the EMG permits the detailed examination of the individual muscle potentials themselves.

JOHNS, New York.

Encephalography, Ventriculography and Roentgenography

AN INVESTIGATION INTO THE CAUSES OF FAILURE OF CERTAIN SUPRATENTORIAL MENINGIOMATA TO SHOW TUMOR VESSELS ON ANGIOGRAPHY. G. MONCKTON, Brain **76**:149 (June) 1953.

Monckton reviews 65 cases of supratentorial meningiomas in an attempt to discern the causes of failure of the tumors to show pathological vessels on angiography. The study is largely a negative one: There is no evidence that the age, sex, length of history, or state of the cardiovascular system was a factor. Results of angiography in 35 tumors in the distribution of the anterior cerebral artery show that the best hope of demonstrating the tumor is by filling the internal carotid artery system; in 20 cases in the distribution of the middle cerebral artery, by filling both internal and external carotid arteries, and in 10 cases in the distribution of the posterior cerebral artery, by injection of the vertebral artery. Plain roentgenograms reveal 29 cases with enlargement of the foramen spinosum, not all having a "corkscrew" middle meningeal arterial groove. Pathologically, 25 of the tumors were stained with benzidine, and

the most vascular architectural types are found to be most easily demonstrated. No cytological correlation is made with the angiographic appearance or results. Physiologically, the "zoning" of contrast medium is not found to be a factor.

Monckton suggests further study to determine the effects of a space-occupying lesion in terms of local stresses upon neighboring vessels, and effects of cerebral perineoplastic edema upon the cerebral circulation.

JOHNS, New York.

Congenital Anomalies

AN UNUSUAL CONGENITAL ANOMALY OF THE BRAIN: AGENESIS OF THE CORPUS CALLOSUM, ABSENCE OF THE SEPTUM PELLUCIDUM, AND FUSION OF THE CEREBRAL HEMISPHERES. W. H. MOSBERG JR. and H. C. VORIS, J. Neuropath. & Exper. Neurol. **13**:369 (April) 1954.

The authors report on a boy who died at the age of 4½ years. It was noted that he was retarded at the age of 7 months, when he was unable to sit up alone. At the age of 3½ years he was unable to sit or walk without support and he could not talk. He appeared to be an alert child and was able to smile and to hold a spoon. The upper extremities showed athetoid movements. The muscle stretch reflexes were generally hypoactive, with bilateral sustained ankle clonus. The Babinski sign was absent. Autopsy revealed the brain to be fused anteriorly in one mass without disruption of the gyral pattern in the midline until 11 cm. posterior to the frontal poles. The gyral pattern was anomalous. Anteriorly there was a single midline ventricle, and the third ventricle appeared to be a continuation of the cavity. There was no evidence of lamina terminalis. There was no corpus callosum. The temporal horn was shortened. The internal capsule and the cerebral peduncles were rudimentary. There was no histologic evidence of Betz cells in the motor cortex. It appeared likely that development was arrested early in fetal life.

SIEKERT, Rochester, Minn.

News and Comment

THE MYASTHENIA GRAVIS FOUNDATION, INC.

The Myasthenia Gravis Foundation, Inc., New York Academy of Medicine, will hold a conference on Myasthenia Gravis on Dec. 8 and 9, 1954, at the University of Pennsylvania School of Medicine, Philadelphia. Both physicians and students are welcome.

All communications should be addressed to 2 E. 103d St., New York 29.

NOTICE

The Annual Meeting of the American Medical Association will be held in Atlantic City, June 6-10, 1955. Physicians hoping to take part in that meeting should communicate with their Section officers as early as possible. Deadlines have been set, after which applications will be considered only if there are withdrawals in the program.

DEADLINE FOR SECTION PAPERS, Dec. 15, 1954

DEADLINE FOR SCIENTIFIC EXHIBIT, Jan. 10, 1955

Communications should be addressed to the following:

Section on Nervous and Mental Diseases

Secretary—Karl O. Von Hagen, M.D., 2010 Wilshire Blvd., Los Angeles 57, Calif.

Representative to Scientific Exhibit—G. Wilse Robinson Jr., M.D., 2625 The Paseo, Kansas City 8, Mo.

Books

In Honour of S. Ramón y Cajal on the Centenary of His Birth 1952. Acta physiologica scandinavica, Supplement 106, Volume 29. Pp. 651. P. E. Norstedt & Söner, Tryckerigatan 2, Stockholm 2, 1952.

This supplement of *Acta physiologica scandinavica* is contributed by members of a research group in neurophysiology in honor of the centenary of Ramón y Cajal's birth. There are thirty-one separate articles on various aspects of neurophysiology. Of these, thirteen deal with the tracts and reflex connections in the spinal cord, three with the brain stem, and seven with the receptor peripheral nerves and nerve roots; three are concerned with the retina; two deal with technical matters, and one is on bladder musculature. A translation of the summaries in Spanish is appended at the end of the volume. This wide range of studies concerned with neurophysiology indeed pays a tribute to the comprehensiveness of Cajal's work in histology, which still serves as a solid basis for investigation in this field.

Epilepsy and the Functional Anatomy of the Human Brain. By Wilder Penfield and Herbert Jasper; Chapter XIV by Francis McNaughton. Price, $16. Pp. 896, with 322 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6, 1954.

This book reports twenty-five years of research on epilepsy at the Montreal Neurological Institute. These twenty-five years have revolutionized the study of epilepsy. Penfield and Jasper have led a remarkable team of investigators, clinical, physiological, and anatomical, who have been in the forefront during this period. Their work not only has thrown light on the nature of the epileptic process in the brain, but has advanced the knowledge of the physiology and anatomy of the brain itself. Great progress has been made in the localization of cerebral function. Especially interesting are observations made by Penfield in the operating room upon the temporal lobe. Stimulation of the temporal cortex in some of his epileptic patients produced

"psychical hallucinations" which seemed to be vivid recollections of past events, unfolding like a dream while the electrode was stimulating the temporal cortex. This discovery of cortical points that can bring back complex memories is unique and of great physiological importance. So far the points have been found only in the temporal cortex of epileptic patients. A step toward the elucidation of the mystery of memory has been made.

Chapters III, IV, and V are especially important for the physiologist, for Penfield and Jasper bring together their clinical, anatomical, and electroencephalographic observations in an effective synthesis. Chapters VI through XIII describe in detail the clinical phenomena of epilepsy. Not only are the bedside observations excellent, but the whole battery of modern surgical and electrical techniques support the fundamental clinical approach. Medical treatment is discussed by McNaughton, in Chapter XIV. There are five other chapters on more technical aspects.

On page 43, the authors state that "the highest level of neuronal integration must be sought in the diencephalon and midbrain." This is a bold prediction. It seems to this reviewer more exact to call this the central integrating system rather than to elevate it with such titles as "highest" or "final." In attempting to describe psychophysiological mechanisms, one must be careful in choosing words. Simply expressed, Penfield and Jasper's work on the centrencephalic system gives the neurologist a new set of observations which fit in with the recent studies of the "feed-back" circuits in the brain. "Integration" appears to be even more complicated than the cerebral connections conceived by Sherrington. It will be decades before details are worked out. In the meanwhile one can argue endlessly about "higher," "lower," and "final" functions. One might ask: "In a great hospital is the integrator in the director's office 'higher' than the perceptive researcher in the laboratory?" One doubts it; but at least he has the final word!

The volume is beautifully illustrated and printed. One can imagine Hughlings Jackson's pleasure if he could have read it. He would have approved of the case histories and philosophical approach to data. He could not fail to have been delighted with the corroboration by complex new methods of many of his astute theories based on clinical experience.

The Process of Psychotherapy. By Harrington V. Ingham, M.D., and Leonore R. Love, Ph.D. Price, $5.00. Pp. 270. McGraw-Hill Book Company, Inc., 330 W. 42d St., New York 36, 1954.

As the title implies, unlike the majority of books on the subject of psychotherapy, this one deals primarily with procedure—hence, very few references to authors, dynamic interpretation of personality cut to the bone, and a great deal of detailed treatment of "what goes on" in psychotherapy. By accentuating "synthesis," no sensitive partisan toes are stepped upon; each psychiatric school can recognize in the text itself, and the leitmotif of its message is the widening of the area of agreement, the gathering of the common denominators all under the banner of plain sense. The patient material employed consists mainly of the young adult population of a large university.

The book is divided into fifteen chapters. The first chapters analyze the role of the therapy and the therapist and the rational, as well as the irrational, aspects of the relationship. The middle part deals with the use to which the therapist puts this relationship in an aim to promote insight, and, finally, the authors lay down their views on psychotherapeutic planning and on the utilization of adjuncts. The last two chapters consist of verbal reproductions of case history dialogues, one more complete than the other, with parenthetical comments of the therapist as he moves along. This is a carefully thought-out, well-written book that would be easier, more agreeable reading if the text were to be broken up into more paragraphs and if it were devoid of so many homespun philosophical remarks. The authors' fear of controversy also bleaches some of the color out of an otherwise useful handbook that will appeal equally to specialists and non-specialists.

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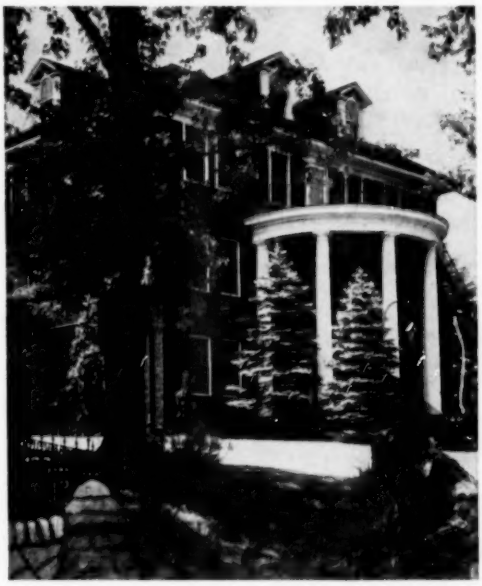

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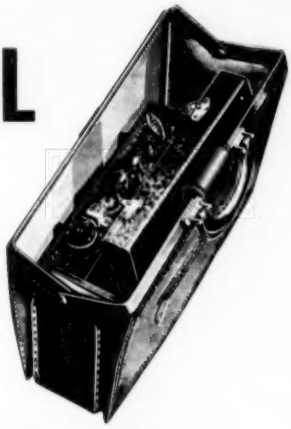

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